

10/798,664

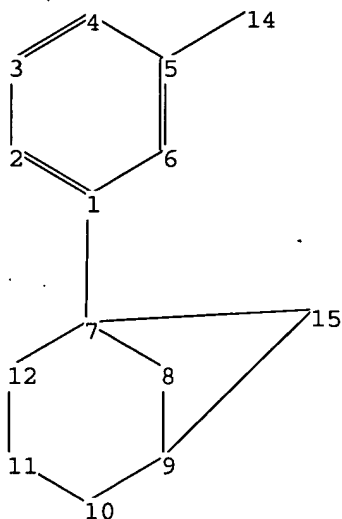
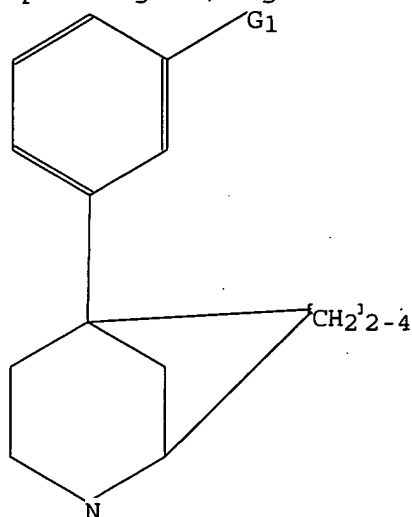
***** STN Columbus *****

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chain nodes :

14

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 15

chain bonds :

1-7 5-14

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 7-15 8-9 9-10 9-15 10-11 11-12

exact/norm bonds :

5-14 7-8 7-12 7-15 8-9 9-10 9-15 10-11 11-12

exact bonds :

1-7

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

G1:C,O,N

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 14:CLASS 15:Atom

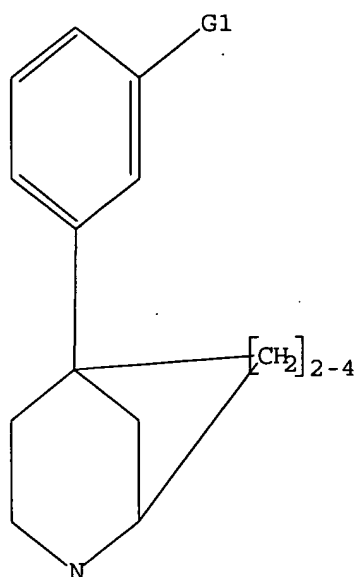
L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

10/798,664



G1 C,O,N

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full

L4 431 SEA SSS FUL L1

=> file ca

=> s l4

L5 55 L4

=> d ibib abs fhitstr 1-55

L5 ANSWER 1 OF 55 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 142:233377 CA
TITLE: Pharmaceutical composition and method using a combination of an opioid receptor antagonist and an $\alpha 2\delta$ ligand for the prevention and treatment of addiction in a mammal
INVENTOR(S): Coe, Jotham Vadvorth; Iredale, Philip A.; McHardy, Stanton Furst; McLean, Stafford
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005043345	A1	20050224	US 2004-870821	20040617
WO 2005018670	A1	20050303	WO 2004-1B2602	20040809

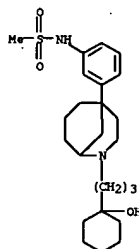
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPL. INFO.: US 2003-497372P P 20030822
AB Pharmaceutical compns. are disclosed for the treatment of alc. or cocaine dependence or addiction, tobacco dependence or addiction, reduction of alc. withdrawal symptoms or aiding in the cessation or lessening of alc. use or substance abuse or other behavioral dependencies including gambling. The pharmaceutical compns. are comprised of a therapeutically effective combination of an opioid receptor antagonist and an $\alpha 2\delta$ ligand and a pharmaceutically acceptable carrier. The method of using these compns. is also disclosed.

IT 774240-03-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(opioid receptor antagonist- $\alpha 2\delta$ ligand combination for prevention and treatment of addiction)

RN 774240-03-8 CA
CN Methanesulfonamide, N-[3-[2-[3-(1-hydroxycyclohexyl)propyl]-2-azabicyclo[3.3.1]non-5-yl]phenyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 1 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)



L5 ANSWER 2 OF 55 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 142:233372 CA
TITLE: Pharmaceutical composition using a combination of an opioid receptor antagonist and a CB-1 receptor antagonist for the prevention and treatment of addiction in a mammal
INVENTOR(S): Coe, Jotham Vadvorth; Iredale, Philip A.; McHardy, Stanton Furst; McLean, Stafford
PATENT ASSIGNEE(S): Pfizer Inc, USA
SOURCE: U.S. Pat. Appl. Publ., 25 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005043327	A1	20050224	US 2004-870209	20040617
WO 2005018645	A1	20050303	WO 2004-1B2596	20040809

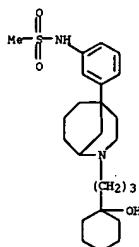
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPL. INFO.: US 2003-496803P P 20030821
AB Pharmaceutical compns. are disclosed for the treatment of alc. or cocaine dependence or addiction, tobacco dependence or addiction, reduction of alc. withdrawal symptoms or aiding in the cessation or lessening of alc. use or substance abuse or other behavioral dependencies including gambling. The pharmaceutical compns. are comprised of a therapeutically effective combination of an opioid receptor antagonist and a CB-1 receptor antagonist and a pharmaceutically acceptable carrier. The method of using these compns. is also disclosed.

IT 774240-03-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(opioid receptor antagonist-CB-1 receptor antagonist combination for prevention and treatment of addiction)

RN 774240-03-8 CA
CN Methanesulfonamide, N-[3-[2-[3-(1-hydroxycyclohexyl)propyl]-2-azabicyclo[3.3.1]non-5-yl]phenyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 2 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)

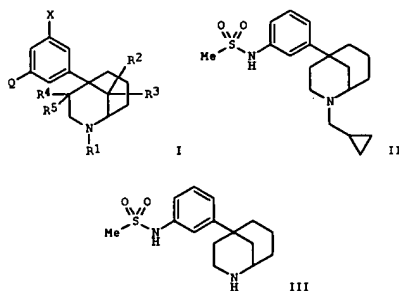


10/798,664

L5 ANSWER 3 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 141:366131
 TITLE: A preparation of 2-azabicyclo[3.3.1]nonane derivatives useful as opioid receptor antagonists
 INVENTOR(S): Coe, Jotham Wadsworth; McHardy, Stanton Furst
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA
 SOURCE: PCT Int. Appl., 45 pp.
 CODEN: PIXKD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089909	A1	20041021	WO 2004-1B1237	20040402
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SV, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

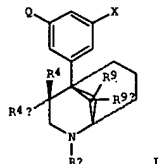
PRIORITY APPLN. INFO.: US 2003-462605P P 20030414
 OTHER SOURCE(S): MARPAT 141:366131
 GI



L5 ANSWER 4 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 141:350040
 TITLE: Preparation of 2-azabicyclo[3.3.1]nonane derivatives as modulators of opioid receptors
 INVENTOR(S): Coe, Jotham W.; McHardy, Stanton
 PATENT ASSIGNEE(S): Pfizer Inc., USA
 SOURCE: U.S. Pat. Appl. Publ., 27 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004204445	A1	20041014	US 2004-762730	20040122

PRIORITY APPLN. INFO.: US 2003-462604P P 20030414
 OTHER SOURCE(S): MARPAT 141:350040
 GI



AB The title compds. [I: R₁ = H, (CH₂)_nCR₁R₂R₃; X = H, halogen, cyano, -C(=O)R₃, C1-4 alkyl group optionally substituted with from one to three halogen atoms; Q = H, halogen, C1-6 alkyl, cyano, NH(C1-4 alkyl), N(C1-4 alkyl)₂, CONH₂, CONH(C1-4 alkyl), CON(C1-4 alkyl)₂, -NHCHO, NHCOR₈, NHSO₂R₈; R₁, R₂ = H, , each (un)substituted C1-6 alkyl, -(CH₂)_j-aryl, -(CH₂)_j-heteroaryl (wherein alkyl, aryl, or heteroaryl is optionally substituted); with the carbon to which R₁ and R₂ are attached, R₁ and R₂ form an (un)substituted C3-7 carbocyclic or 4- to 7-membered heterocyclic group; R₃ is absent or is H, C1-4 alkyl optionally containing

one or two unsatd. bonds, OH, C1-4 alkoxy, hydroxy-C1-4 alkyl, (CH₂)_n-NR₁₀aR₁₀b, -(CH₂)_n-NHCOC(C1-4 alkyl), -(CH₂)_n-NO₂, -(CH₂)_n-CN, -(CH₂)_n-CONH₂, (CH₂)_n-CONH(C1-4 alkyl), -(CH₂)_n-CONR₁₀aR₁₀b; R₃a = H, C1-6 alkyl optionally substituted with one or more halogen; R₄, R₅, R₉a = H, C1-4 alkyl, C1-4 alkoxy; R₈ = H, C1-6 alkyl, C3-6 cycloalkyl, aryl, -(C2-C4 alkyl)-O-(C1-4 alkyl), aryl, -(CH₂)_n-NR₁₀aR₁₀b, 4- to 7-membered heterocyclic; R₁₀a, R₁₀b, R₁₄, R₁₅ = H, C1-4 alkyl; or R₁₀a and R₁₀b or R₁₄ and R₁₅ connect to form a 4-7 membered heterocyclic ring; R₁₄, R₁₅ = H, C1-6 alkyl; j, n = independently an integer from 0 to 5] are prepared. These compds. bind to and modulate (i.e., inhibit, partially inhibit, activate or partially activate) an opioid receptor or receptors in a mammal, including a human. The subject invention also relates to pharmaceutical compns. comprising such derivs. and methods of using such derivs. to treat disease states, disorders and conditions mediated by opioid receptors, which are selected from the group consisting of

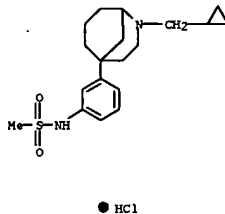
L5 ANSWER 3 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)
 AB The invention relates to a preparation of 2-azabicyclo[3.3.1]nonane derivs. of

formula I [wherein: Q is H, halogen, alkyl, CN, NH₂, or NHCHO, etc.; X is H, halogen, CN, or C(=O)R₃, etc.; R₁ is H, (CH₂)₀-5Me, or (CH₂)₀-5CH(alkyl)(alkyl), etc.; R₂, R₃, R₄, and R₅ are independently selected from H, alkyl, or alkoxy], useful for the treatment of diseases, disorders, and conditions mediated by opioid receptors. The invention relates to the treatment of irritable bowel syndrome, drug addiction, including alc. addiction, and depression, etc. For instance, 2-azabicyclo[3.3.1]nonane derivative II was prepared via reductive alkylation of

III by cyclopropylcarboxaldehyde. I were determined in assays to possess K_i values of about 80 or less for the μ opioid receptor.

IT 774240-02-7P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of 2-azabicyclo[3.3.1]nonane derivs. useful as opioid receptor antagonists)

RN 774240-02-7 CA
 CN Methanesulfonamide, N-[3-[2-(cyclopropylmethyl)-2-azabicyclo[3.3.1]non-5-yl]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



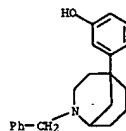
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)
 Irritable bowel syndrome, constipation, nausea, vomiting, pruritic dermatoses, psoriasis, eczema, insect bite, eating disorder, depression, anxiety, schizophrenia, drug addiction, opioid overdose, sexual dysfunction, stroke, head trauma, traumatic brain injury, spinal damage, Parkinson's disease, Alzheimer's disease, age-related cognitive decline and attention deficit, and hyperactivity disorder. In a μ opioid receptor binding assay to rat forebrain tissue, most of the compds. I, e.g. N-[3-[2-(cyclopropylmethyl)-2-azabicyclo[3.3.1]non-5-yl]phenyl]methanesulfonamide hydrochloride, tested at 100 nM were found to inhibit [3H]-DAMGO binding at the μ opioid receptor in a range of 10-100n.

IT 774239-89-3P, 3-(2-Benzyl-2-azabicyclo[3.3.1]non-5-yl)phenol
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of 2-azabicyclo[3.3.1]nonane derivs. as modulators of opioid receptors for treatment of disease states, disorders, and conditions mediated by opioid receptors)

RN 774239-89-3 CA
 CN Phenol, 3-[2-(phenylmethyl)-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)



L5 ANSWER 5 OF 55 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:
TITLE:

AUTHOR(S):

CORPORATE SOURCE:

SOURCE:

PUBLISHER:

DOCUMENT TYPE:

LANGUAGE:

OTHER SOURCE(S):

GI

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141:225716 CA

Probes for Narcotic Receptor-Mediated Phenomena.
33. Construction of a Strained trans-5,6-Ring System by
Displacement of a Nitro-Activated Aromatic Fluorine.
Synthesis of the Penultimate Oxide-Bridged
PhenylmorphansHashimoto, Akihiro; Przybyl, Anna K.; Linders, Joannes
T. M.; Kodato, Shinichi; Tian, Xinrong; Deschamps,
Jeffrey R.; George, Clifford; Flippen-Anderson, Judith
L.; Jacobson, Arthur E.; Rice, Kenner C.Laboratory of Medicinal Chemistry, National Institute
of Diabetes, Digestive and Kidney Diseases, National
Institutes of Health, Bethesda, MD, 20892-0815, USA

Journal of Organic Chemistry (2004), 69(16), 5322-5327

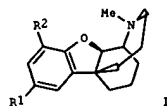
CODEN: JOCEAH; ISSN: 0022-3263

American Chemical Society

Journal

English

CASREACT 141:225716



AB The synthesis of the ortho- and para- isomers I (R1 = HO, R2 = H; R1 = H, R2 = HO) in the oxide-bridged 5-phenylmorphane series of rigid tetracyclic compds. was accomplished via racemic 5-(2-fluoro-5-nitrophenyl)-2-methyl-2-azabicyclo[3.3.1]nonan-9-ol, an intermediate containing an aromatic nitro-activated fluorine atom. The fluorine atom was used as the leaving group for the formation of the strained tetracyclic trans-fused 5,6-ring system in racemic (1a,4a,9a)-1,3,4,9a-tetrahydro-2-methyl-6-nitro-2H-1,4a-propanobenzofuro[2,3-c]pyridine (±)-I (R1 = O2N; R2 = H), although preference for cis ring fusion during the formation of tricyclic tetra- and hexahydrodibenzofurans has been well-documented. Single-crystal X-ray crystallog. study of the desired para- isomer (±)-I (R1 = HO; R2 = H), as well as of two intermediates in its synthesis, provided assurance of the correct structures. The e-isomers are among the last of the 12 oxide-bridged 5-phenylmorphans to be synthesized. These rigid, tetracyclic compds. were synthesized in order to determine the three-dimensional pattern of a ligand that would enable interaction with opioid receptors as agonists or antagonists.

IT 746639-16-7P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(crystal structure; preparation of oxide-bridged phenylmorphans with a
strained trans-5,6-ring system using nucleophilic substitution reaction
of nitro-activated aromatic fluorine)

RN 746639-16-7 CA

CN 2-Azabicyclo[3.3.1]nonan-9-ol, 5-(2-fluoro-5-nitrophenyl)-2-methyl-

L5 ANSWER 6 OF 55 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

TITLE:

AUTHOR(S):

CORPORATE SOURCE:

SOURCE:

PUBLISHER:

DOCUMENT TYPE:

LANGUAGE:

OTHER SOURCE(S):

AB

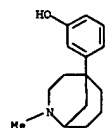
The opioid receptor binding affinities of N-methyl- and N-phenethyl-5-phenylmorphans with a meta-hydroxy substituent [3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)phenol, and 3-(2-phenethyl-2-azabicyclo[3.3.1]non-5-yl)phenol] were compared with the affinities of four new ligands bearing an ortho- or para-hydroxyl substituent [2-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)phenol and 2-(2-phenethyl-2-azabicyclo[3.3.1]non-5-yl)phenol, 4-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)phenol, and 4-(2-phenethyl-2-azabicyclo[3.3.1]non-5-yl)phenol] that were synthesized from 2-bromoanisole or the known 2-methyl-5-phenyl-2-azabicyclo[3.3.1]nonane, resp. The data indicated that either the electronic state of the phenolic ring is critical for the ligand's interaction with an opioid receptor, or that there must be a specific distance and angle for a hydrogen bond between the phenolic moiety and an amino acid in the binding domain that cannot be altered.

IT 27107-68-2

RL: PAC (Pharmacological activity); BIOL (Biological study)
(critical structural determinant of opioid receptor interaction with
phenolic 5-phenylmorphans)

RN 27107-68-2 CA

CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

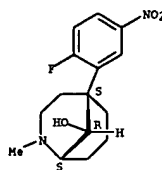
27

THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)

monohydrobromide, (1R,5R,9S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



• HBr

REFERENCE COUNT:

28

THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 55 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

TITLE:

AUTHOR(S):

CORPORATE SOURCE:

SOURCE:

PUBLISHER:

DOCUMENT TYPE:

LANGUAGE:

OTHER SOURCE(S):

AB

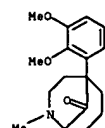
In an attempt to obtain the para- isomer, rac-(1R,4aR,9aR)-2-methyl-1,3,4,9a-tetrahydro-2H-1,4a-propanobenzofuro[2,3-c]pyridin-6-ol, via mesylation of an intermediate 9a-hydroxyphenylmorphane, we obtained, instead, a rearranged chloro compound with a 5-membered nitrogen ring, 7-chloro-3a-(2,5-dimethoxyphenyl)-1-methyl-octahydroindole. This indole underwent a second rearrangement to give us the desired para- isomer. The structures of the intermediate indole and the final product were unequivocally established by X-ray crystallog. A resynthesis of the known rac-(1R,4aR,9aR)-2-methyl-1,3,4,9a-tetrahydro-2H-1,4a-propanobenzofuro[2,3-c]pyridin-6-ol, the ortho- isomer, was achieved using the reaction conditions for the para- isomer, as well as under Mitsunobu reaction conditions where, unusually, the oxide-bridge ring in the 5-phenylmorphane was closed to obtain the desired product. The synthesis of the para- isomer adds an addnl. compound to those oxide-bridged phenylmorphans that were initially visualized and synthesized; the establishment of the structure and configuration of 8 of the theor. possible 12 racemates has now been achieved. The X-ray crystallog. structure anal. of the para- isomer provides essential data that will be needed to establish the configuration of a ligand necessary to interact with an opioid receptor.

IT 231289-74-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of para-f oxide-bridged phenylmorphane)

RN 231289-74-0 CA

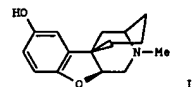
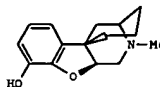
CN 2-Azabicyclo[3.3.1]nonan-9-one, 5-(2,3-dimethoxyphenyl)-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)



• HCl

15 ANSWER 7 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)
 REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

15 ANSWER 8 OF 55 CA COPYRIGHT 2005 ACS on STN
 139:246129 CA
 ACCESSION NUMBER:
 TITLE: Probes for narcotic receptor mediated phenomena. Part
 31: Synthesis of rac-(3R,6aS,11aS)-2-methyl-
 1,3,4,5,6,11a-hexahydro-2H-3,6a-methanobenzofuro[2,3-
 c]azocine-10-ol, and azocine-8-ol, the ortho-c and the
 para-c oxide-bridged phenylmorphans isomers
 Tadic, Dragana; Lindero, Joannes T. M.;
 Flippen-Anderson, Judith L.; Jacobson, Arthur E.;
 Rice, Kenner C.
 CORPORATE SOURCE: Department of Health and Human Services, Laboratory of
 Medicinal Chemistry, National Institutes of Health,
 National Institute of Diabetes and Digestive and
 Kidney Diseases, Bethesda, MD, 20892-0815, USA
 SOURCE: Tetrahedron (2003), 59(25), 4603-4614
 CODEN: TETRA; ISSN: 0040-4020
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 139:246129
 GI

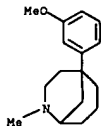


AB Two of the 12 possible oxide-bridged phenylmorphans, were synthesized, rac-(3R,6aS,11aS)-2-methyl-1,3,4,5,6,11a-hexahydro-2H-3,6a-methanobenzofuro[2,3-c]azocine-10-ol (I) (the ortho-c compound), and rac-(3R,6aS,11aS)-2-methyl-1,3,4,5,6,11a-hexahydro-2H-3,6a-methanobenzofuro[2,3-c]azocine-8-ol (II) (the para-c compound). Single-crystal X-ray diffraction studies indicated that the dihedral angle between the least squares planes through the Ph ring and the atoms C1, C11a, C12, and C3 in the piperidine ring in both I·CHCl₃ and II·HBr was 6.9°. The C12-C6a-C6b-C10a torsion angle was found to be 139.3° for both compds. The angular relationship between the phenolic ring and the piperidine ring in phenylmorphans that interact with specific opioid receptors as agonists or antagonists is of considerable theor. interest.

IT 53661-47-5
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (synthesis of rac-(3R,6aS,11aS)-2-Me-1,3,4,5,6,11a-hexahydro-2H-3,6a-methanobenzofuro[2,3-c]azocine-10-ol, and azocine-8-ol, the ortho-c and the para-c oxide-bridged phenylmorphans isomers as opioid receptor probes)

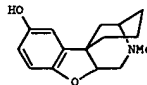
RN 53661-47-5 CA
 CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

15 ANSWER 8 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

15 ANSWER 9 OF 55 CA COPYRIGHT 2005 ACS on STN
 139:53181 CA
 ACCESSION NUMBER:
 TITLE: Probes for narcotic receptor mediated phenomena. Part
 30. Synthesis of rac-(3R,6aS,11aR)-1,3,4,5,6,11a-hexahydro-2-methyl-2H-3,6a-methanobenzofuro[2,3-c]azocin-8-ol, an epoxy isomer of 5-phenylmorphans
 Lindero, Joannes T. M.; Mirsadeghi, Seid;
 Flippen-Anderson, Judith L.; George, Clifford;
 Jacobson, Arthur E.; Rice, Kenner C.
 CORPORATE SOURCE: Laboratory of Medicinal Chemistry, National Institute
 of Diabetes and Digestive and Kidney Diseases,
 National Institutes of Health, Bethesda, MD,
 20892-0815, USA
 SOURCE: Helvetica Chimica Acta (2003), 86(2), 484-493
 CODEN: HCACTV; ISSN: 0018-019X
 PUBLISHER: Verlag Helvetica Chimica Acta
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 139:53181
 GI



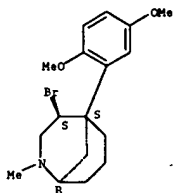
AB The synthesis of a series of epoxy 5-phenylmorphans is being explored in order to determine the conformational requirements of the phenolic ring in a phenylmorphans mol. that may be needed both for binding to a specific opioid receptor and for exhibiting opioid agonist or antagonist activity. Of the twelve possible ortho- and para-bridged isomers, the authors now report the synthesis of the para-d isomer, rac-(3R,6aS,11aR)-2-methyl-1,3,4,5,6,11a-hexahydro-2H-3,6a-methanobenzofuro[2,3-c]azocin-8-ol (I). Compound I was synthesized via construction of the 5-phenylazabicyclo[3.3.1]non-3-ene skeleton and subsequent closure of the epoxy bridge. As determined by an X-ray diffraction study, the epoxy bridge, restricting the phenyl-ring rotation, fixed the dihedral angle between the least-squares planes through the Ph ring and atoms N(2), C(3), C(11a), and C(6a) of the piperidine ring at 43.0°, and the torsion angle C(12)-C(6a)-C(6b)-C(10a) at -95.0°.

IT 546101-00-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (synthesis of rac-(3R,6aS,11aR)-1,3,4,5,6,11a-hexahydro-2-methyl-2H-3,6a-methanobenzofuro[2,3-c]azocin-8-ol, an epoxy isomer of 5-phenylmorphans as probe for narcotic receptor mediated phenomena)

RN 546101-00-2 CA
 CN 2-Azabicyclo[3.3.1]nonane, 4-bromo-5-(2,5-dimethoxyphenyl)-2-methyl-, (1R,4S,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L5 ANSWER 9 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 55 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 138:265113 CA
TITLE: Probes for Narcotic Receptor Mediated Phenomena. Part 28: New Opioid Antagonists from Enantiomeric Analogs of 5-(3-Hydroxyphenyl)-N-phenylethylmorphans

AUTHOR(S): Hashimoto, Akihiro; Jacobson, Arthur E.; Rothman, Richard B.; Dersch, Christina M.; George, Clifford; Flippen-Anderson, Judith L.; Rice, Kenner C.
CORPORATE SOURCE: National Institute of Diabetes and Digestive and Kidney Diseases, Laboratory of Medicinal Chemistry, National Institutes of Health, Bethesda, MD, 20892-0815, USA

SOURCE: Bioorganic & Medicinal Chemistry (2002), 10(10), 3319-3329
CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 138:265113

AB Enantiomeric analogs of 5-(3-hydroxyphenyl)morphans ligands were synthesized and evaluated because of our unexpected finding that opioid antagonists can be obtained in the 5-phenylmorphans series of opioids without sterically hindering the rotation of the phenolic ring. We determined the opioid receptor binding affinity of these new analogs, as well as the efficacy of the more interesting ligands.

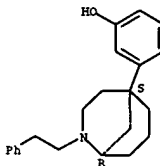
IT 330625-46-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (preparation and structure activity relations of enantiomeric analogs of (hydroxyphenyl)phenylethylmorphans as opioid antagonists)

RN 330625-46-2 CA

CN Phenol, 3-[(1R,5S)-2-(2-phenylethyl)-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 55 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 137:155089 CA
TITLE: Preparation of azabicyclononanes for therapeutic use as κ opioid receptor ligands for the treatment of cocaine or heroin addiction

INVENTOR(S): Carroll, F. Ivy; Thomas, James B.; Mascarella, S. Wayne

PATENT ASSIGNEE(S): Research Triangle Institute, USA

SOURCE: PCT Int. Appl., 57 pp.

CODEN: PIXKD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060445	A1	20020808	WO 2002-US1231	20020201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SH, TD, TG				
US 2002143145	A1	20021003	US 2001-774566	20010201
US 6559159	B2	20030506		
CA 2436409	AA	20020808	CA 2002-2436409	20020201
EP 1363629	A1	20031126	EP 2002-704144	20020201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004520383	T2	20040708	JP 2002-560637	20020201
PRIORITY APPLN. INFO:			US 2001-774566	A 20010201
			WO 2002-US1231	W 20020201

OTHER SOURCE(S): MARPAT 137:155089
GI

L5 ANSWER 11 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)

binding of the κ opioid receptor, such as heroin or cocaine addictions. Thus, amide II was prepd. via a multistep synthetic sequence which included cyclization of (S)-1,2,3,6-tetrahydro-1,3-dimethyl-4-[3-(1-methylethoxy)phenyl]pyridine with Okahara's reagent, i.e. ClCH₂C(OCH₂OMe):CH₂, to form the azabicyclononane core. The prepd. azabicyclononanes were assayed for κ opioid receptor binding activity.

IT 444903-94-0

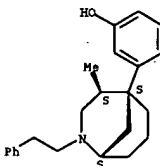
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of azabicyclononanes for therapeutic use as κ opioid receptor ligands for the treatment of cocaine or heroin addiction)

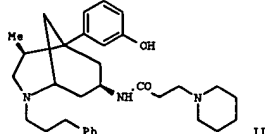
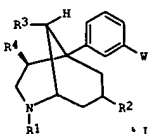
RN 444903-94-0 CA

CN Phenol, 3-[(1S,4S,5S)-4-methyl-2-(2-phenylethyl)-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



AB Structurally novel κ opioid receptor antagonists, such as I [R1 = alkyl, alkenyl, alkynyl, arylalkyl, etc.; R2 = acylamino, carbamoyl, carbonyl, aminoalkyl, heterocyclylalkyl, etc.; R3 = H, alkyl, alkenyl, alkynyl, arylalkyl, carbonyl; R4 = H, alkyl, alkenyl, alkynyl, arylalkyl; W = H, OH, acyloxy, amino, sulfonylamino, acylamino], were prepared for therapeutic use in treatment of disease states that are ameliorated by

L5 ANSWER 12 OF 55 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:
TITLE:

134:231497 CA
Opioid peptide receptor studies. 14. Stereochemistry determines agonist efficacy and intrinsic efficacy in the [35S]GTP-γ-S functional binding assay
XU, Heng; Hashimoto, Akibiro; Rice, Kenner C.; Jacobson, Arthur E.; Thomas, James B.; Carroll, F. Ivy; Lai, Josephine; Rothman, Richard B.
CPS, DIR, NIDA, Baltimore, MD, 21224, USA
Synapse (New York) (2001), 39(1), 64-69
CODEN: SYNART; ISSN: 0887-4476
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

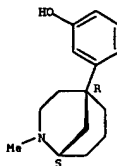
AB Previous data obtained with the cloned rat μ opioid receptor demonstrated that stereochem. affects the four parameters of the ligand-receptor interaction: potency (ED50), efficacy (maximal stimulation), intrinsic efficacy (effect as a function of receptor occupation), and binding affinity. This study evaluated the activities of structurally diverse opioid receptor ligands in the [35S]GTP-γ-S binding assay, comparing the relationship between receptor binding, activation, efficacy, and intrinsic efficacy. The data, obtained with cloned rat μ receptors, demonstrated that an analgetic, (-)-5-m-hydroxyphenyl-2-methylmorphinan (NIH8508), and its (+)-isomer (NIH8509), behave as partial agonists, but had different intrinsic efficacy in the [35S]GTP-γ-S binding assay. Replacement of the Me group with the phenethyl group on the piperidine nitrogen of NIH8508 and NIH8509 [(1R,5S)-AH019 and (1S,5R)-AH019] increased affinity for the μ receptor and eliminated any agonist effect, supporting the hypothesis that certain structural features make these compds. antagonists. These study also show that all of the fully efficacious μ agonists studied here had high levels of intrinsic efficacy, producing a 50% response at about 10% receptor occupancy. Comparison of the binding Ki in competitively inhibiting [125I]OXY binding to the functional Ki for opioid antagonists [Ki(1OXY)/Ki(GTP-γ-S)] provides more detailed evidence that the [35S]GTP-γ-S binding assay can be used to reliably determine apparent functional antagonist Ki values in addition to agonist ED50, efficacy and intrinsic efficacy.

IT 20623-81-6, NIH 8509
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(opioid peptide receptor studies. 14. stereochem. det. agonist efficacy and intrinsic efficacy in the [35S]GTP-γ-S functional binding assay)

RN 20623-81-6 CA
CN Phenol, 3-[(1S,5R)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L5 ANSWER 12 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 55 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:
TITLE:

131:228652 CA
Preparation of substituted piperidines for pharmaceutical use as opioid antagonists
Carroll, Frank Ivy
USA
PCT Int. Appl., 171 pp.
CODEN: PIXX02

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945925	A1	19990916	WO 1999-US5131	19990309
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, NG, SN, TD, TG				
CA 2324418	AA	19990916	CA 1999-2324418	19990309
AU 9930738	A1	19990927	AU 1999-30738	19990309
AU 756983	B2	20030130		
EP 1061919	A1	20001227	EP 1999-912345	19990309
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002506032	T2	20020226	JP 2000-535340	19990309
EP 1512683	A1	20050309	EP 2004-100891	19990309
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 6900228	B1	20050531	US 2000-623872	19990309
US 2002165396	A1	20021107	US 2002-100097	20020319
US 6552032	B2	20030422		
US 2002169324	A1	20021114	US 2002-100096	20020319
US 6593348	B2	20030715		
US 2002193602	A1	20021219	US 2002-99948	20020319
US 6531481	B2	20030311		
US 2003158415	A1	20030821	US 2002-266774	20021009
US 2004146518	A1	20040729	US 2003-742782	20031223
PRIORITY APPL. INFO.:			US 1998-77402P	P 19980310
			US 1998-107902P	P 19981110
			EP 1999-912345	A3 19990309
			WO 1999-US5131	W 19990309
			US 2000-623872	A3 20001127
			US 2002-99948	A1 20020319

OTHER SOURCE(S): MARPAT 131:228652
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Piperidine containing heterocyclic compds. I [R1, R2 = H, alkyl, aryl, arylalkyl; R3 = alkyl, cycloalkyl, aryl, arylalkyl, etc.], II [R1 = alkyl, arylalkyl; R3, R4, R5, R6 = H, OH, NH2, CN, CF3, CN, NO2, alkyl, alkoxy,

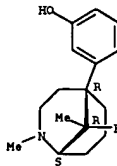
L5 ANSWER 13 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)

halogen, amino, etc.; R7 = H, alkyl], and III [R1 = alkyl, arylalkyl; R2 = H, NH2, OH, alkyl, arylalkyl, amino, etc.] were prepd. for use as opioid antagonists to treat a variety of disease states which involve the opioid receptors. Thus, the hydrochloride salt of piperidine IV [R3 = (CH2)2C6H4-4-OH], i.e. RTI 5989-29, was prepd. starting from (+)-(3R,4R)-dimethyl-4-(3-hydroxyphenyl)piperidine, N-(tert-butoxycarbonyl)-L-valine, and 3-(4-hydroxyphenyl)propanoic acid. The prepd. heterocyclic compds. contg. a piperidine subunit were tested for κ-, μ-, and δ-opioid receptor binding activity.

IT 244048-54-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic compds. containing a piperidine subunit for pharmaceutical use as opioid antagonists)

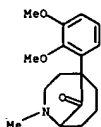
RN 244048-54-2 CA
CN Phenol, 3-[(1R,5S,9S)-2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

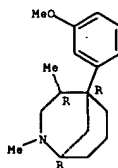
L5 ANSWER 14 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 131:102160 CA
 TITLE: An expedient synthesis of 9-keto-2-methyl-5-(dimethoxyphenyl)morphans
 AUTHOR(S): Linders, Joannes T. M.; Flippen-Anderson, Judith L.; George, Clifford F.; Rice, Kenner C.
 CORPORATE SOURCE: Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0815, USA
 SOURCE: Tetrahedron Letters (1999), 40(20), 3905-3908
 CODEN: TETLEA; ISSN: 0040-4039
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 131:102160
 AB An expedient synthesis of ortho-methoxy substituted 9-keto-5-phenylmorphans has been developed, featuring a Thorpe-Ziegler cyclization to construct the substituted 2-phenylcyclohexanone intermediate.
 IT 231289-74-09
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of (dimethoxyphenyl)morphan derivs.)
 RN 231289-74-0 CA
 CN 2-Azabicyclo[3.3.1]nonan-9-one, 5-(2,3-dimethoxyphenyl)-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 130:182632 CA
 TITLE: A stereoselective synthetic approach to N-alkyl-4 β -methyl-5-phenylmorphans
 AUTHOR(S): Thomas, James B.; Gigstad, Kenneth M.; Fix, Scott E.; Burgess, Jason P.; Cooper, Julie B.; Mascarella, S. Wayne; Cantrell, Buddy E.; Zimmerman, Dennis M.; Carroll, F. Ivy
 CORPORATE SOURCE: Chemistry and Life Sciences, Research Triangle Institute, Research Triangle Park, NC, 27709, USA
 SOURCE: Tetrahedron Letters (1999), 40(3), 403-406
 CODEN: TETLEA; ISSN: 0040-4039
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 130:182632
 AB A convergent, highly stereoselective synthetic approach to N-alkyl-4 β -methyl-5-phenylmorphans has been developed utilizing alkylation of the metalloenamine of N-alkyl-1,2,3,6-tetrahydro-4-phenylpyridines with 2-(chloromethyl)-3,5-dioxahex-1-ene (Okahara's reagent) followed by Clemmensen reduction
 IT 220503-24-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (a stereoselective synthetic approach to N-alkyl-4 β -methyl-5-phenylmorphans)
 RN 220503-24-2 CA
 CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)-2,4-dimethyl-, (1R,4R,5R)- (9CI) (CA INDEX NAME)

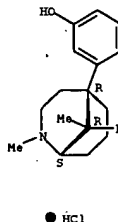
Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 129:325731 CA
 TITLE: N-Substituted 9 β -Methyl-5-(3-hydroxyphenyl)morphans Are Opioid Receptor Pure Antagonists
 AUTHOR(S): Thomas, James B.; Zheng, Xisoling; Mascarella, S. Wayne; Rothman, Richard B.; Dersch, Christina M.; Partilla, John S.; Flippen-Anderson, Judith L.; George, Clifford F.; Cantrell, Buddy E.; Zimmerman, Dennis M.; Carroll, F. Ivy
 CORPORATE SOURCE: Chemistry and Life Sciences, Research Triangle Institute, Research Triangle Park, NC, 27709, USA
 SOURCE: Journal of Medicinal Chemistry (1998), 41(21), 4143-4149
 CODEN: JMCMAH; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The inhibition of radioligand binding and [35S]GTP γ S functional assay data for N-methyl- and N-phenethyl-9 β -methyl-5-(3-hydroxyphenyl)morphans (I and II) show that these compds. are pure antagonists at the μ , δ , and κ opioid receptors. Since I and II have the 5-(3-hydroxyphenyl) group locked in a conformation comparable to an equatorial group of a piperidine chair conformation, this information provides very strong evidence that opioid antagonists can interact with opioid receptors in this conformation. In addition, it suggests that the trans-3,4-dimethyl-4-(3-hydroxyphenyl)piperidine class of antagonist operates via a Ph equatorial piperidine chair conformation. Importantly, the close relationship between the 4-(3-hydroxyphenyl)piperidines and 5-(3-hydroxyphenyl)morphan antagonists shows that the latter class of compound provides a rigid platform on which to build a novel series of opioid antagonists.
 IT 215124-71-3P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation and opioid receptor antagonist activity of N-substituted 9 β -methyl-5-(3-hydroxyphenyl)morphans)
 RN 215124-71-3 CA
 CN Phenol, 3-[(1R,5S,9S)-2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl]-, hydrochloride, rel- (9CI) (CA INDEX NAME)
 Relative stereochemistry.

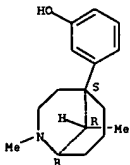
L5 ANSWER 16 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

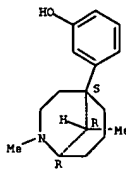
L5 ANSWER 17 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 125:185593 CA
 TITLE: Dependence studies of new compounds in the rhesus monkey, rat and mouse (1995)
 AUTHOR(S): Aceto, M. D.; Bowman, E. R.; Harris, L. S.; May, E. L.
 CORPORATE SOURCE: Medical College Virginia, Virginia Commonwealth University, Richmond, VA, USA
 SOURCE: NIDA Research Monograph (1996), 162(Problems of Drug Dependence, 1995), 408-451
 CODEN: MIDAD4; ISSN: 0361-8595
 PUBLISHER: National Institute on Drug Abuse
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The ability of a series of drugs to produce dependence was studied in rhesus monkeys, rats, and mice.
 IT 88550-29-2
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (dependence studies of new compds. in rhesus monkey and rat and mouse)
 RN 88550-29-2 CA
 CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, anti- (9CI) (CA INDEX NAME)

Relative stereochemistry.

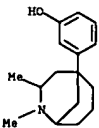


L5 ANSWER 18 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 125:185591 CA
 TITLE: Biological evaluation of compounds for their physical dependence potential and abuse liability. XIX. Drug evaluation committee of the College on Problems of Drug Dependence, Inc. (1995)
 AUTHOR(S): Jacobson, A. E.
 CORPORATE SOURCE: Laboratory Medicinal Chemistry, National Institute Diabetes Digestive Kidney Diseases, Bethesda, MD, USA
 SOURCE: NIDA Research Monograph (1996), 162(Problems of Drug Dependence, 1995), 363-376
 CODEN: MIDAD4; ISSN: 0361-8595
 PUBLISHER: National Institute on Drug Abuse
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The phys. dependence potential and abuse liability of various analgesics and stimulants and depressants is described and related to their biol. activities.
 IT 88550-29-2
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (therapeutic use); BIOL (Biological study); USES (Uses) (biol. evaluation of compds. for phys. dependence potential and abuse liability of analgesics and stimulants and depressants)
 RN 88550-29-2 CA
 CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, anti- (9CI) (CA INDEX NAME)

Relative stereochemistry.

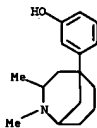


L5 ANSWER 19 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 125:132417 CA
 TITLE: Biological evaluation of compounds for their physical dependence potential and abuse liability. XVII. Drug Evaluation Committee of the College on Problems of Drug Dependence, Inc. (1993)
 AUTHOR(S): Jacobson, A. E.
 CORPORATE SOURCE: USA
 SOURCE: NIDA Research Monograph (1994), 140(Problems of Drug Dependence 1993, Vol. 1), 179-195
 CODEN: MIDAD4; ISSN: 0361-8595
 PUBLISHER: National Institute on Drug Abuse
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The Drug Evaluation Committee (DEC) of the CPDD (Dr. T. Cicero, Chairman) is charged with the responsibility of determining the phys. dependence potential and abuse liability of potential analgesics, stimulants, and depressants, and with associated methodol. research. The drugs are obtained from investigators in universities, industrial groups, and the public sector. The testing function is carried out under the auspices of the CPDD as a public service and has provided information to pharmaceutical industry and governmental agencies for the appropriate scheduling of a drug with the potential for abuse. The information which DEC provides to university researchers, who frequently work under a NIDA grant, is useful for determining the desirability of structural modification of a drug and the DEC biol. data are often needed for publication of their work in medicinal chemical journals. Data are reported for 61 compds.
 IT 178896-97-4, NIH 10779
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (biol. evaluation of drugs for their phys. dependence potential and abuse liability)
 RN 178896-97-4 CA
 CN Phenol, 3-(2,3-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride (9CI) (CA INDEX NAME)



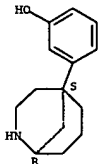
● HCl

L5 ANSWER 20 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 125:104826 CA
 TITLE: Dependence studies of new compounds in the rhesus monkey, rat and mouse (1994)
 AUTHOR(S): Aceto, M.D.; Bowman, E.R.; Harris, L.S.; May, E.L.
 CORPORATE SOURCE: USA
 SOURCE: NIDA Research Monograph (1995), 152(Problems of Drug Dependence 1994, Vol. 1), 162-212
 CODEN: MIDAD4; ISSN: 0361-8595
 PUBLISHER: National Institute on Drug Abuse
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Twenty-eight compds. were examined in rhesus monkey, rat, and mouse for antinociceptive activity, ability to substitute for morphine, and development of phys. dependence. The data acquired were compared with several standard drugs.
 IT 178896-97-4, NIH 10779
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (dependence studies of new compds. in the rhesus monkey, rat and mouse)
 RN 178896-97-4 CA
 CN Phenol, 3-(2,3-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride (9CI) (CA INDEX NAME)

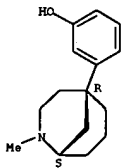


● HCl

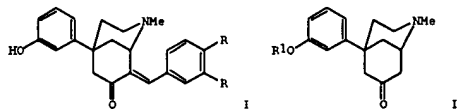
L5 ANSWER 21 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 123:218718 CA
 TITLE: Ligand selectivity of cloned human and rat opioid μ receptors
 AUTHOR(S): Brothman, Richard B.; Xu, Heng; Wang, Jia Bei; Partilla, John S.; Kayakiri, Hiroshi; Rice, Kenner C.; Uhl, George R.
 CORPORATE SOURCE: Clinical Psychopharmacology Section, Laboratory of Medicinal Chemistry, Baltimore, MD, 21224, USA
 SOURCE: Synapse (New York) (1995), 21(1), 60-4
 CODEN: SYNART; ISSN: 0887-4476
 PUBLISHER: Wiley-Liss
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Opiate receptors play major roles in analgesic and euphoric effects of opiate drugs. Recent cloning of cDNAs encoding the rodent and human μ receptor revealed high homol. between the predicted receptors but also some sequence differences. To determine if these sequence differences produced significant changes in ligand-selectivity profiles, the authors assessed these profiles in expressing COS and CHO cell lines using the agonist ligand [125I]DXY-AGO (5 β -[125Iodo]-3,14-dihydroxy-17-methyl-4,5 α -epoxymorphinan). This ligand's high specific activity (2200 Ci/mmol) and high affinity for μ opioid receptors generated high signal-to-noise ratio binding. The resulting ligand-selectivity profiles of the human and rat μ receptors reveal modest differences in affinities for morphine and naloxone in COS cells but not CHO cells. Ligand-selectivity profiles of the rat and human μ receptors were otherwise similar. Interesting differences between these data and data previously obtained with the peptide agonist [3H]DAMGO suggest that the peptide and alkaloid agonists may label different domains of the μ receptor.
 IT 168135-17-9
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 CN 168135-17-9 CA
 RN Phenol, 3-[(1R,5S)-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)
 Absolute stereochemistry. Rotation (-).



L5 ANSWER 22 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)

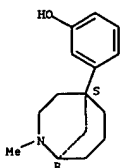


L5 ANSWER 22 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 122:23041 CA
 TITLE: Probes for Narcotic Receptor-Mediated Phenomena. 20. Alteration of Opioid Receptor Subtype Selectivity of the 5-(3-Hydroxyphenyl)morphans by Application of the Message-Address Concept: Preparation of δ -Opioid Receptor Ligands
 AUTHOR(S): Bertha, Craig M.; Flippen-Anderson, Judith L.; Rothman, Richard B.; Porreca, Frank; Davis, Peg; Xu, Heng; Becketts, Karen; Cha, Xian-Yuan; Rice, Kenner C.
 CORPORATE SOURCE: Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 20892, USA
 SOURCE: Journal of Medicinal Chemistry (1995), 38(9), 1523-37
 CODEN: JMCHAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Derivs. of racemic and optically active 5-(3-hydroxyphenyl)-2-methylmorphans (5-(3-hydroxyphenyl)-2-methyl-2-azabicyclo[3.3.1]nonane; 1) were synthesized containing addnl. aromatic moieties, as an application of the message-address concept targeted at producing δ -opioid receptor selective ligands. In vitro radioreceptor binding studies in rat brain revealed that both of the parent enantiomers, (-)- and (+)-1, had a high affinity for the μ -opioid receptor (21 nM), a slight affinity for κ -opioid receptors (.apprx.800-900 nM), and less than 1000 nM affinity for the δ -opioid receptor (μ / δ IC50 ratio of <0.02 for both). A derivative of (-)-1 containing an indole moiety fused at the C6-C7 position of the phenylmorphans nucleus, (-)-II, displayed a >180-fold increase in affinity for the δ -opioid receptor with an IC50 value of 6 nM. The parent compound (-)-I had only 26% agonist activity at 30 μ M in the mouse vas deferens (δ) bioassay, whereas compound (-)-II had an IC50 of 393 nM in this preparation, indicating the importance of the indole moiety in imparting δ -opioid agonist activity to the phenylmorphans (-)-1. A structural relation (SAR) study of N-alkyl derivs. of the racemic nor II indicated similarities between the interaction of various derivs. with the μ - and δ - but not the κ -opioid receptor. As studies on the mol. basis of the interaction of opioid ligands with their resp. receptors continue to gain momentum, the structure activity data described herein for the synthetic phenylmorphans will prove useful for further studies.
 IT 28623-81-6
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 CN 28623-81-6 CA
 RN Phenol, 3-[(1S,5R)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)
 Absolute stereochemistry. Rotation (+).

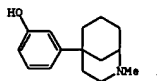


AB The (E)-8-benzylidene and (E)-8-(3,4-dichlorobenzylidene), 7-ketone derivs., I (R = H, Cl), of the synthetic opiate 2-methyl-5-(3-hydroxyphenyl)morphans [5-(3-hydroxyphenyl)-2-methyl-2-azabicyclo[3.3.1]nonane], were synthesized from II (R1 = H, Me) via the Claisen-Schmidt reaction. The corresponding enantiomers of I were obtained in >99% optical purity from the optical isomers of II (R1 = H), resolved with the O,O'-dibenzoyltartaric acids. The absolute configurations of the enantiomers of II (R1 = H) were determined. The determination of the regioisomer and configurational isomer of I (R = H), with respect to the introduced benzylidene group, was determined from a single-crystal x-ray anal. 1H NMR data was used to confirm that I (R = Cl) possessed the same configuration as I (R = H). Radioreceptor binding studies in rat and guinea pig brain preps. revealed that (-)-(1S,5S)-I (R = H) displayed an 11-fold decrease in affinity for the opioid μ receptor and an increase in affinity for κ receptors of 81-fold (low nanomolar affinity) relative to the ketone precursor (+)-(1S,5S)-II (R1 = H). An analogous, albeit less dramatic, trend was seen with compound (-)-(1S,5S)-I (R = Cl). Compds. (-)-(1S,5S)-I (R = H) and (-)-(1S,5S)-I (R = Cl) are distinct from the typical α -opiates in that they have very low affinity for either PCP sites or muscarinic receptors. The high affinity and selectivity of these novel α receptor ligands suggests that they will be valuable for the elucidation of the functional roles of α receptors.
 IT 28623-84-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 CN 28623-84-9 CA
 RN Phenol, 3-[(1R,5S)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

L5 ANSWER 23 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).



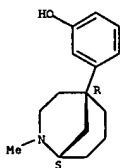
L5 ANSWER 24 OF 55 CA COPYRIGHT 2005 ACS on STN
120:125 CA
ACCESSION NUMBER:
TITLE: Conformational analysis of the opioid phenylmorphinan and its 9a-methyl analog in solution using high-resolution nuclear magnetic resonance spectroscopy
AUTHOR(S): DiMeglio, Christine M.; Froimowitz, Mark; Makriyannis, Alexandros
CORPORATE SOURCE: Sch. Pharm., Univ. Connecticut, Storrs, CT, 06269, USA
SOURCE: Pharmaceutical Research (1993), 10(8), 1200-5
CODEN: PHREED; ISSN: 0724-8741
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB The solution conformations of the opioid phenylmorphinan (I, R = H) and its 9a-Me analog (II) were studied using 1- and 2-dimensional (2-D) high resolution NMR techniques. The NMR spectra were analyzed by interpreting the phase-sensitive 2-D COSY and double quantum filtered COSY spectra, 1H-1H vicinal coupling consts., and NOE effects in the phase-sensitive 2-D NOESY spectra. For both compds., a chair-chair conformation of the cyclohexane and piperidine rings is exclusively preferred with some distortion of the rings from perfectly staggered chairs. For phenylmorphans, the Ph ring is oriented to fit into the cleft formed by the cyclohexane and piperidine rings. Thus, for the (+)-enantiomer, the Ph group assumes the same orientation with regard to the piperidine ring as morphine consistent with the morphine-like properties of the compound. For the Me analog, the plane of the Ph ring essentially bisects the piperidine ring to which it is attached and is outside of the required range of opioid agonists. This is consistent with the atypical properties of the 2 enantiomers. The NMR results are compared to the conformations of (-)-phenylmorphinan and the (+)-9a-Me analog in the crystal state and to the results of mol. mechanics studies.
IT 28623-81-6
RL: PRP (Properties)
(conformation of, in solns., NMR study of)
RN 28623-81-6 CA
CN Phenol, 3-[(1S,5R)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

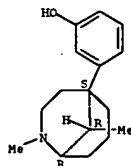
Absolute stereochemistry. Rotation (+).

L5 ANSWER 24 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)



L5 ANSWER 25 OF 55 CA COPYRIGHT 2005 ACS on STN
118:256 CA
ACCESSION NUMBER:
TITLE: Absolute configuration and conformation of the pure opioid antagonist (+)-2,9a-dimethyl-5-(m-hydroxyphenyl)morphinan
AUTHOR(S): Froimowitz, Mark; Pangborn, Walter; Cody, Vivian
CORPORATE SOURCE: Alcohol Drug Res. Cent., McLean Hosp., Belmont, MA, 02178-9106, USA
SOURCE: Chirality (1992), 4(6), 377-83
CODEN: CHALEP; ISSN: 0899-0042
DOCUMENT TYPE: Journal
LANGUAGE: English
AB (+)-2,9a-Dimethyl-5-(m-hydroxyphenyl)morphinan is the only phenylmorphinan analog whose affinity for opioid κ -receptors is greater than its affinity for opioid μ -receptors. Pharmacol., the compound is a pure opioid antagonist devoid of agonist activity in in vivo assays of antinociception. The absolute configuration of the compound has been determined to be (1R,5S,9R) from an X-ray crystallog. study of the chloride salt. Thus, the absolute configuration corresponds to that of the atypical opioid agonist (-)-phenylmorphinan while the weak atypical agonist (-)-2,9a-dimethyl-5-(m-hydroxyphenyl)morphinan corresponds to the potent morphine-like (+)-phenylmorphinan. The preferred orientations of the Ph ring for the two stereoisomers were determined using the mol. mechanics program MM2-87 and found to vary from that of the two parent compds. The atypical properties of the two 9a-Me analogs is consistent with an opioid ligand model which proposes that morphine-like properties require a particular range of Ph orientations. There was good agreement between the structure obtained from X-ray crystallog. and computed with the MM2-87 program.
IT 88550-31-6
RL: PRP (Properties)
(configuration and conformation of, crystal structure in relation to)
RN 88550-31-6 CA
CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride, anti-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



● HCl

L5 ANSWER 26 OF 55 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

116:227659 CA

TITLE:

Phenylmorphans and analogs: opioid receptor subtype

AUTHOR(S):

Froimowitz, Mark; Pick, Chaim G.; Pasternak, Gavril W.

CORPORATE SOURCE:

Alcohol Drug Abuse Res. Cent., McLean Hosp., Belmont,

MA, 02178, USA

SOURCE:

Journal of Medicinal Chemistry (1992), 35(9), 1521-5

CODEN: JMCMAH; ISSN: 0022-2623

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB The morphine-like (+)-phenylmorphans, the atypical (-)-enantiomer, and some analogs were tested in receptor binding assays selective for opioid μ_1 , μ_2 , κ , κ_1 , and κ_3 receptors. The affinities of all of the compds. except one, including the atypical (-)-phenylmorphans, were greatest for μ_1 and μ_2 receptors. The only exception was the (+)-9a-Me analog which had slightly greater affinity for the κ_1 receptor. The selective receptor binding assays provide evidence that opioids in which the Ph ring is constrained to be equatorial on the piperidine ring can have considerable affinity for μ receptors. In addition, the analgesic dose-response curves were determined for (+)- and (-)-phenylmorphans using the mouse tail-flick assay with the (+)-enantiomer being 7-fold more potent. Pretreatment with the selective opioid antagonists β -FNA (μ_1 and μ_2), naloxonazine (μ_1), nor-ENI (κ_1), and naltrindole (κ) suggests that the antinociceptive activity of both enantiomers is mediated through μ receptors. The pretreatment with naloxonazine, which attenuated the antinociceptive effect, shows that both (+)- and (-)-phenylmorphans are μ_1 agonists, while intrathecal administration shows that both are μ_2 agonists. Conformational energy calcs. on the compds. were also performed using the MM2-87 program. Consistent with previous conformational results for the phenylmorphans, the most potent antinociceptive compds. preferred a particular orientation of the Ph ring.

IT 28623-81-6

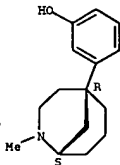
RL: BIOL (Biological study)

(analgesic activity and opioid receptor subtype selectivity of)

RN 28623-81-6 CA

CN Phenol, 3-[(1S,5R)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 27 OF 55 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

114:135894 CA

TITLE:

Evaluation of new compounds for opioid activity

AUTHOR(S):

Woods, J.; Medzihradsky, F.; Smith, C.; Winger, G.;

France, C.

CORPORATE SOURCE:

USA

SOURCE:

NIDA Research Monograph (1988), 90(Probl. Drug

Depend., 1988), 421-67

CODEN: NIDADA; ISSN: 0361-8595

DOCUMENT TYPE:

Journal; General Review

LANGUAGE:

English

AB The opioid activity of different compds. tested in different exptl. systems are described.

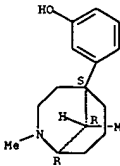
IT 88550-32-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (opioid activity of, evaluation of)

RN 88550-32-7 CA

CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, anti-(-)- (9CI) (CA INDEX NAME)

Rotation (-). Absolute stereochemistry unknown.



L5 ANSWER 26 OF 55 CA COPYRIGHT 2005 ACS on STN

(Continued)

ACCESSION NUMBER:

112:111859 CA

TITLE:

Correction of: 109:86100

AUTHOR(S):

Biological evaluation of compounds for their physical

CORPORATE SOURCE:

dependence potential and abuse liability. X. Drug

testing programs of the Committee on Problems of Drug

Dependence, Inc. (1986)

SOURCE:

Jacobson, Arthur E.

Lab. Chem., Natl. Inst. Diabetes Dig. Kidney Dis.,

Bethesda, MD, 20892, USA

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB A report is given on the drug-testing programs of the Committee on Problems of Drug Dependence, and new and lit. data are presented from studies of the dependency potential of a large number of drugs, including epoxymorphinans, phenylmorphans, benzomorphans, methadone-like compds., pethidines, fentanyl, etc.

IT 88550-29-2

RL: PRP (Properties)

(abuse and dependence potential of)

RN 88550-29-2 CA

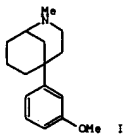
CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, anti- (9CI) (CA

INDEX NAME)

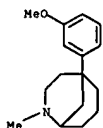
Relative stereochemistry.



L5 ANSWER 29 OF 55 CA COPYRIGHT 2005 ACS ON STN
 ACCESSION NUMBER: 110:8444 CA
 TITLE: Functionalized 2-azabicyclo[3.3.1]nonanes. VIII. New synthesis of 5-phenylmorphans
 AUTHOR(S): Bonjoch, Josep; Casamitjana, Nuria; Bosch, Joan
 CORPORATE SOURCE: Fac. Pharm., Univ. Barcelona, Barcelona, 08028, Spain
 SOURCE: Tetrahedron (1988), 44(6), 1735-41
 CODEN: TETRA8; ISSN: 0040-4020
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 110:8444
 GI

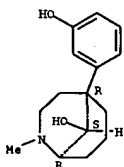


AB A new procedure for the synthesis of 2-azabicyclo[3.3.1]nonanes, e.g. I, by intramol. cyclization of 4-acetonyl-2-piperidinocarbonitriles under acidic conditions is described. The procedure allows the preparation of the pharmacol. interesting 5-phenylmorphans and involves the initial formation of 1-methyl-4-acetonylidene-piperidine, conjugate addition of a diaryl-cuprate, and cyclization of the resulting 4-acetonylpiperidine by way of the corresponding 2-cyano derivative
 IT 53661-47-5p
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 53661-47-5 CA
 CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



L5 ANSWER 31 OF 55 CA COPYRIGHT 2005 ACS ON STN
 ACCESSION NUMBER: 105:183743 CA
 TITLE: Evaluation of new compounds for opioid activity (1985)
 AUTHOR(S): Woods, James H.; Medzihradsky, Fedor; Smith, Charles B.; Winger, Gail D.; Gmerek, Debra E.
 CORPORATE SOURCE: Dep. Pharmacol., Univ. Michigan, Ann Arbor, MI, 48109-0010, USA
 SOURCE: NIDA Research Monograph (1986), 67(Probl. Drug Depend.), 453-89
 CODEN: MIDAD4; ISSN: 0361-8595
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The opioid-like activity of 36 compds. (benzomorphans, xylidines, morphinans, peptides, phenylpiperazines, etc.) was evaluated and the data were summarized in this report. The test procedures included drug discrimination, dependence liability, and i.v. self-administration in monkeys, displacement of [3H]etorphine from rat cerebral membranes, and inhibition of twitch in elec. driven guinea pig ileum and mouse vas deferens.
 IT 95689-23-9
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (opioid activity of)
 RN 95689-23-9 CA
 CN Benzeneacetic acid, α -hydroxy-, compd. with syn-5-(3-hydroxyphenyl)-2-methyl-2-azabicyclo[3.3.1]nonan-9-ol (1:1) (9CI) (CA INDEX NAME)
 CH 1
 CRN 95689-22-8
 CMF C15 H21 N O2

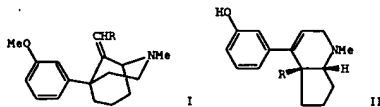
Relative stereochemistry.



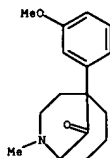
CH 2
 CRN 90-64-2
 CMF C9 H8 O3



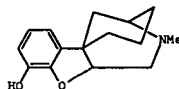
L5 ANSWER 30 OF 55 CA COPYRIGHT 2005 ACS ON STN
 ACCESSION NUMBER: 106:196223 CA
 TITLE: Hexahydro-1H-1-pyridines from acid rearrangement of 9-alkylidene-5-(m-methoxyphenyl)-2-methylmorphans. Structural type of narcotic antagonists
 AUTHOR(S): Awaya, Hiroyoshi; May, Everette L.; Aceto, Mario D.; Harris, Louis S.; Silverton, James V.; Rice, Kenner C.; Mattson, Mariena V.; Jacobson, Arthur E.
 CORPORATE SOURCE: Dep. Pharmacol., Med. Coll. Virginia, Richmond, VA, 23298, USA
 SOURCE: Journal of Medicinal Chemistry (1987), 30(5), 947-50
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 106:196223
 GI



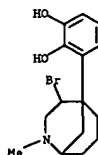
AB 9-Methylene- and 9-ethylidene-5-(m-methoxyphenyl)-2-methylmorphans I and refluxing 48% HBr gave rearrangement products II (R = H, Me). The structure of II (R = Me) was determined by x-ray crystallog. and that of II (R = H) follows from analogy and NMR data. The II are opioid antagonists of about the potency of nalorphine.
 IT 88550-34-9
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (Wittig reaction of, with ethylphosphonium salt)
 RN 88550-34-9 CA
 CN 2-Azabicyclo[3.3.1]nonan-9-one, 5-(3-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



L5 ANSWER 32 OF 55 CA COPYRIGHT 2005 ACS ON STN
 ACCESSION NUMBER: 104:186678 CA
 TITLE: Probes for narcotic receptor mediated phenomena. 9. Synthesis of (±)-(3 α ,6 α ,11 α)-1,3,4,5,6,11a-hexahydro-2-methyl-2H-3,6a-methanobenzofuro[2,3-c]azocin-10-ol, and oxide-bridged 5-(m-hydroxyphenyl)morphans
 AUTHOR(S): Burke, Terrence R., Jr.; Jacobson, Arthur E.; Rice, Kenner C.; Weissman, Ben Avi; Huang, Hsueh Cheng; Silverton, J. V.
 CORPORATE SOURCE: Lab. Chem., Natl. Inst. Arthritis, Metab. Dig. Kidney Dis., Bethesda, MD, 20205, USA
 SOURCE: Journal of Medicinal Chemistry (1986), 29(5), 748-51
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 104:186678
 GI

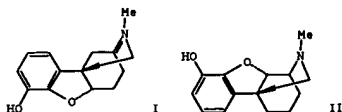


AB The title compound [(±)-I] was prepared and showed low binding to rat brain homogenate receptor preps.
 IT 100448-08-6p
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and cyclization of)
 RN 100448-08-6 CA
 CN 1,2-Benzenediol, 3-(4-bromo-2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrobromide (9CI) (CA INDEX NAME)



• HBr

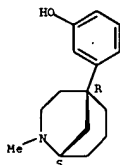
L5 ANSWER 33 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 102:160031 CA
 TITLE: Probes for narcotic receptor mediated phenomena 3.
 Oxide bridged 5-phenylmorphans
 AUTHOR(S): Burke, Terrence R., Jr.; Jacobson, Arthur E.; Rice,
 Kenner C.; Weissman, Ben Avi; Silverton, James V.
 CORPORATE SOURCE: Lab. Chem., NIH, MD, USA
 SOURCE: NIDA Research Monograph (1984), 49, 109-13
 CODEN: MIDAD4; ISSN: 0361-8595
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



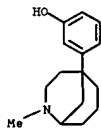
AB Oxide bridged 5-phenylmorphans (I and II) were prepared and tested for analgesic activity as well as opiate receptor binding properties. The phenylmorphans had no analgesic activity. II exhibited appreciable binding to rat brain homogenate. Structural requirement of the drugs binding to opiate receptors is discussed.

IT 28623-81-6
 RL: PROC (Process)
 (analgesic activity and opiate receptor binding of)
 RN 28623-81-6 CA
 CN Phenol, 3-[(1S,5R)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 34 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)



L5 ANSWER 34 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 102:159988 CA
 TITLE: Demonstration and affinity labeling of a stereoselective binding site for a benzomorphan opiate on acetylcholine receptor-rich membranes from Torpedo electroplaque
 AUTHOR(S): Oswald, Robert E.; Penrow, Nancy N.; McLaughlin, James T.
 CORPORATE SOURCE: New York State Coll. Vet. Med., Cornell Univ., Ithaca, NY, 14853, USA
 SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1985), 82(3), 940-4
 CODEN: PNASA6; ISSN: 0027-8424
 DOCUMENT TYPE: Journal
 LANGUAGE: English

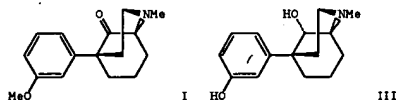
AB The interaction of an optically pure benzomorphan opiate, (-)-N-allyl-N-normetazocine [(-)-ANMC] [14198-28-8], with the nicotinic acetylcholine receptor from Torpedo electroplaque was studied by using radioligand binding and affinity labeling. The binding was complex with at least 2 specific components having equilibrium dissociation constants of 0.3 μ M and 2 μ M. The affinity of the higher affinity component was decreased by carbamoylcholine [462-58-8] but not by α -bungarotoxin [11032-79-4]. The effect of carbamoylcholine was not blocked by α -bungarotoxin. In comparison, the affinity of [3H]phenylcyclidine [77-10-1], a well-characterized ligand for a high-affinity site for noncompetitive blockers on the acetylcholine receptor, is increased by carbamoylcholine and the increase is blocked by α -bungarotoxin. The binding of (-)-[3H]ANMC was inhibited by a number of other benzomorphanes, with (-)-isomers being 4- to 5-fold more potent than (+)-isomers. Phenylcyclidine inhibits the binding of (-)-[3H]ANMC to its high-affinity site by a mechanism that is not competitive. UV-catalyzed affinity labeling indicated that the high-affinity-binding site for (-)-[3H]ANMC is at least partially associated with the δ subunit. Tryptic degradation of the Torpedo marmorata δ chain suggested that (-)-ANMC labeled a 16,000-dalton COOH-terminal portion of the subunit. In contrast, 5-azido(trimethisoquin) [75041-53-1], a photoaffinity label of the high-affinity site for noncompetitive blockers, labels a 47,000-dalton NH2-terminal fragment of the δ subunit. Thus, (-)-[3H]ANMC binds to sites completely distinct from the binding sites for acetylcholine. The high-affinity-binding site for (-)-ANMC and that for phenylcyclidine and 5-azido(trimethisoquin) are allosterically coupled but are regulated differently and are probably phys. distinct.

IT 27107-68-2
 RL: BIOL (Biological study)
 (normetazocine binding to acetylcholine receptor rich membrane response to, in Torpedo electroplaque)
 RN 27107-68-2 CA
 CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)

IT 27107-68-2
 RL: BIOL (Biological study)
 (normetazocine binding to acetylcholine receptor rich membrane response to, in Torpedo electroplaque)
 RN 27107-68-2 CA
 CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)

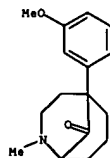
IT 27107-68-2 CA
 CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)

L5 ANSWER 35 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 102:149088 CA
 TITLE: 9 α - and 9 β -hydroxyphenylmorphans
 AUTHOR(S): Aways, Hiroyoshi; May, Everett L.; Jacobson, Arthur E.; Aceto, Mario D.
 CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, 23298, USA
 SOURCE: Journal of Pharmaceutical Sciences (1984), 73(12), 1867-8
 CODEN: JPMSAZ; ISSN: 0022-3549
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



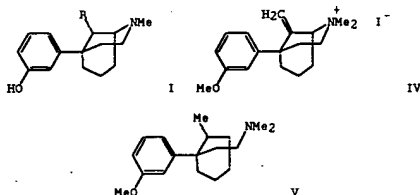
AB Platinum oxide hydrogenation of 5-m-methoxyphenyl-2-methyl-9-oxomorphan (I) gave the 9 α -hydroxy racemate whose phenolic analog (II) is a strong antinociceptive agent, fully supportive of morphine dependence in rhesus monkeys. The di-O-acetyl derivative of II was similar to II in its profile of activity. The diastereoisomer of II, obtained by hydrogenation of the methobromide of I, extrusion of Me bromide, and O-demethylation of the resultant free base, was almost inactive antinociceptively and did not suppress withdrawal symptoms in morphine-dependent monkeys. The orientation of the C-9 hydroxyl groups was deduced from spectral data and by analogy.

IT 88550-34-9
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (hydrogenation of)
 RN 88550-34-9 CA
 CN 2-Azabicyclo[3.3.1]nonan-9-one, 5-(3-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



10/798,664

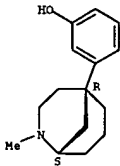
L5 ANSWER 36 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 100:121413 CA
 TITLE: Racemic and optically active 2,9-dimethyl-5-(*m*-hydroxyphenyl)morphans and pharmacological comparison with the 9-demethyl homologs
 AUTHOR(S): Awaya, Hiroyoshi; May, Everette L.; Aceto, Mario D.; Merz, Herbert; Rogers, Michael E.; Harris, Louis S.
 CORPORATE SOURCE: Dep. Pharmacol., Med. Coll. Virginia, Richmond, VA, 23298, USA
 SOURCE: Journal of Medicinal Chemistry (1984), 27(4), 536-9
 CODEN: JMCMAH; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB Dimethyl(hydroxyphenyl)morphane I (R = Me) (II) was prepared from 5-(*m*-methoxyphenyl)-2-methyl-9-oxomorphane and resolved into its enantiomers. The α -orientation of the C-9 Me group was derived from studies of induced NMR shifts. (+)-II has inappreciable agonist (antinociceptive) activity in mice, and (-)-II shows codeine-like potency in the hot-plate and writhing tests only. The 9-demethyl homologs I (R = H) (III) are strong agonists, about as potent as morphine in these tests as well as in the tail-flick assay. (+)-II and (+)-III, but not (-)-I, exhibit low-potency, narcotic-antagonist activity in mice (tail-flick test, vs. morphine). All three precipitate abstinence in nonwithdrawn, morphine-dependent rhesus monkeys. Monkey studies with the 9-demethyl homologs confirmed earlier results showing that (+)-III, suppressing abstinence in withdrawn animals, has high phys. dependence capacity, while (-)-III, has none. Instead, (-)-III induces abstinence in nonwithdrawn animals. Studies in rats and isolated organs (guinea pig ileum and mouse vas deferens) and receptor-binding assays confirm the different opioid-action profiles of (+)-III, and (-)-III which thus might interact with different opioid receptors. Catalytic hydrogenation of the methiodide IV gave, instead of the expected epimer of II, ring-opened compound V.
 IT 88550-34-9
 RL: RCT (Reactant); RACT (Reactant or reagent)
 RN 88550-34-9 CA
 (Wittig reaction of, with methyltriphenylphosphonium iodide)

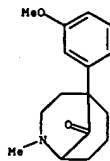
L5 ANSWER 37 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 98:27684 CA
 TITLE: Biological evaluation of compounds for their dependence liability. V. Drug testing program of the Committee on Problems of Drug Dependence, Inc. (1981)
 AUTHOR(S): Jacobson, A. E.
 CORPORATE SOURCE: Lab. Chem., Natl. Inst. Arthritis, Diabetes Dig. Kidney Dis., Bethesda, MD, 20205, USA
 SOURCE: NIDA Research Monograph (1982), Volume Date 1981, 41, 331-7
 CODEN: MIDAD4; ISSN: 0361-8595
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Sixty-three compds. were evaluated for dependence liability.
 IT 27107-49-9
 RL: BIOL (Biological study)
 (dependence on)
 RN 27107-49-9 CA
 CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride, (1S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



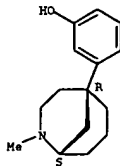
● HCl

L5 ANSWER 36 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)
 CN 2-Azabicyclo[3.3.1]nonan-9-one, 5-(3-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



L5 ANSWER 38 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 97:192941 CA
 TITLE: Dependence studies of new compounds in the rhesus monkey, rat, and mouse (1981)
 AUTHOR(S): Aceto, M. D.; Harris, L. S.; May, E. L.
 CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, 23298, USA
 SOURCE: NIDA Research Monograph (1982), Volume Date 1981, 41, 338-80
 CODEN: MIDAD4; ISSN: 0361-8595
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Sixty-six compds. were tested for dependence in the rhesus monkey, rat, and mouse by various methods.
 IT 27107-49-9
 RL: BIOL (Biological study)
 (dependence on)
 RN 27107-49-9 CA
 CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride, (1S)-(9CI) (CA INDEX NAME)

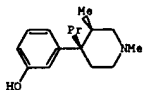
Absolute stereochemistry. Rotation (+).



● HCl

10/798,664

L5 ANSWER 39 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 97155939 CA
 TITLE: Structural requirements for affinity and intrinsic activity at the opiate receptor defined in 4-phenylpiperidine and related series
 AUTHOR(S): Zimmerman, D. M.; Smits, S. E.; Hynes, M. D.; Cantrell, B. E.; Reamer, M.; Nickander, R.
 CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
 SOURCE: NIDA Research Monograph (1982), Volume Date 1981, 41, 112-18
 CODEN: MIDADA; ISSN: 0361-8595
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



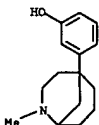
AB The effect of 3-Me substitution in the 4-alkyl-4-phenylpiperidine series was primarily related to a loss of intrinsic activity rather than affinity at the opiate receptor and, as seen with LY 150720 (I) [79201-85-7], this effect can be highly stereospecific. Comparisons of the 1,3,4-trimethyl- with the 1,3,4,6-tetramethyl-4-phenylpiperidines suggest that this loss of intrinsic activity, and resulting narcotic antagonist activity, is mediated through an equatorial-Ph conformational binding mode. Furthermore, the pharmacol. changes arising from 2-Me substitution in the 1,3,4,6-tetramethyl-4-phenylpiperidines appear to be the result of a change induced in the conformational binding mode by steric interactions. The cis-phenylpiperidines, like the 1,3,4-trialkyl-4-phenylpiperidines and the 2-methylphenylmorphans appear to bind to the opiate receptor and exert their pharmacol. actions in the equatorial-Ph binding mode. Consequently, factors affecting receptor affinity and intrinsic activity in these series are related. These results further substantiate the existence and importance of at least 2 distinct binding modes at the opiate receptor postulated by Portoghesi (1965). In the equatorial-Ph binding mode, the 3 position of the piperidine has been characterized as a stereospecific site that alters intrinsic activity, producing antagonist activity.

IT 27107-68-2
 RL: PROC (Process)
 (opiate receptor binding of, mol. structure in relation to)
 RN 27107-68-2 CA
 CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)

L5 ANSWER 40 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 95:204248 CA
 TITLE: Phenylpropylamino groups of morphine analgesics plotted with a computer
 AUTHOR(S): Brouant, P.; Soyfer, J. C.
 CORPORATE SOURCE: Lab. Pharm. Chim., Fac. Pharm., Marseille, F 13385/5, Fr.
 SOURCE: Annales Pharmaceutiques Francaises (1981), 39(2), 125-31
 CODEN: APPRAD; ISSN: 0003-4509
 DOCUMENT TYPE: Journal
 LANGUAGE: French

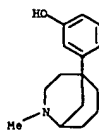
AB The conformational variations of the phenylpropylamino group of morphine and related analgesics were plotted with a computer on the basis of crystallog. data. The analgesic activity was related to the conformational variations.

IT 76580-81-9
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (conformation of phenylpropylamino group in, computer-plotted, analgesic activity in relation to)
 RN 76580-81-9 CA
 CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrobromide (9CI) (CA INDEX NAME)



● HBr

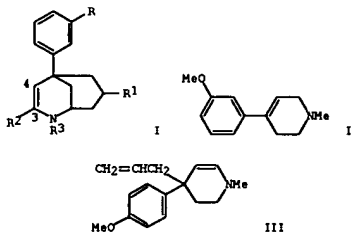
L5 ANSWER 39 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)



L5 ANSWER 41 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 94:83962 CA
 TITLE: Phenylmorphane derivatives
 PATENT ASSIGNEE(S): Eli Lilly and Co., USA
 SOURCE: Jpn. Kokai Tokkyo Koho, 19 pp.
 CODEN: JJKKXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

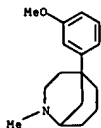
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 55124768	A2	19800926	JP 1980-32566	19800311
FR 2451368	A1	19801010	FR 1980-5179	19800307
FR 2451368	B1	19830318		
EE 882152	A1	19800910	EE 1980-9743	19800310
HU 22162	O	19820428	HU 1980-561	19800310
HU 179836	B	19821228		
CA 1148150	A1	19830614	CA 1980-347364	19800310
EP 18077	A2	19801029	EP 1980-300746	19800311
EP 18077	A3	19801126		
R: DE, GB, NL, SE				
GB 2045248	A	19801029	GB 1980-8172	19800311
GB 2045248	B2	19830505		
EP 59989	A1	19820915	EP 1982-102714	19800311
R: DE, GB, NL, SE				
US 4278797	A	19810714	US 1980-150763	19800519
GB 2111976	A1	19830713	GB 1982-27192	19820923
PRIORITY APPLN. INFO.:				
			US 1979-19527	A 19790312
			EP 1980-300746	A 19800311
			GB 1980-8172	A3 19800311

OTHER SOURCE(S): CASREACT 94:83962
 GI



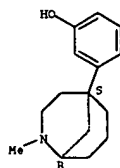
AB Phenylmorphane derivs. (I; R = H, OH, C1-3 alkoxy; R1, R2 = H, C1-5 alkyl, C3-5 alkenyl, R1 = R2 = H; R3 = H, C1-10 alkyl, aryl, C3-10 alkenyl, cycloalkylmethyl; 3,4-saturated or unsatd.), effective analgesics at 0.5-29.0

L5 ANSWER 41 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)
 mg/kg in mice, were prepd. Thus, 1.6 mol BuLi was added to a soln. of
 24.36 g II in THF at 0° with stirring followed by CH₂CHCH₂Br in
 Et₂O at -50° to give 17.91 g III, which (1.0 g) was cyclized in aq.
 H₃PO₄-HCO₂H at 24° to give 950 mg I (R = MeO, R₁ = R₂ = H, R₃ = Me,
 3,4-unsatd.).
 IT 53661-47-5P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); SPN (Synthetic preparation); BIOL (Biological
 study); PREP (Preparation)
 (preparation and analgesic activity of)
 RN 53661-47-5 CA
 CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)-2-methyl- (9CI) (CA INDEX
 NAME)



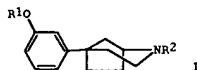
L5 ANSWER 42 OF 55 CA COPYRIGHT 2005 ACS on STN
 93:132662 CA
 TITLE: Radiocrytalographic study of variations in skeletal
 conformation in morphine analgesics
 AUTHOR(S): Brouant, P.; Soyfer, J. C.
 CORPORATE SOURCE: Lab. Pharm. Chim., Fac. Pharm., Marseille, 13385/4,
 Fr.
 SOURCE: Annales Pharmaceutiques Francaises (1979), 37(9-10),
 461-8
 CODEN: APFRAD; ISSN: 0003-4509
 Journal
 DOCUMENT TYPE: French
 LANGUAGE: French
 AB Eight parameters, defined from the crystallog. coordinates, for 21
 analgesics containing the phenylpropylamine group, were based on the
 distance
 between the N atom and a quaternary C atom center, various planes or
 centers in aromatic rings. The distances formed 4 distinct sets which were
 related to their physiol. activity. The conformations of the
 morphine-like analgesics was discussed.
 IT 53467-24-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (conformation and crystal and mol. structure of, analgesic activity in)
 RN 53467-24-6 CA
 CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrobromide, (1R)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

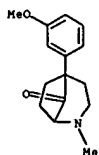


● HBr

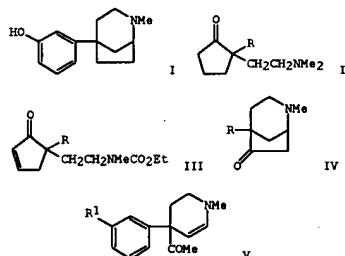
L5 ANSWER 43 OF 55 CA COPYRIGHT 2005 ACS on STN
 89:99709 CA
 TITLE: Synthesis and analgetic activity of some
 5-aryl-2-azabicyclo[3.2.1]octanes
 AUTHOR(S): Ong, Helen R.; Anderson, V. B.; Wilker, Jeffrey C.
 CORPORATE SOURCE: Chem. Res. Dep., Hoechst-Roussel Pharm., Inc.,
 Somerville, NJ, USA
 SOURCE: Journal of Medicinal Chemistry (1978), 21(8), 758-63
 CODEN: JMCMAJ; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB 26 Title compds. I (R₁ = H, Me, or Ac; R₂ = alkyl, PhCH₂CH₂, substituted
 phenylethyl, thienylethyl, etc.) were synthesized and evaluated for
 analgesic agonist-antagonist activity. Several of the compds. had
 analgesic potency comparable to morphine in the mouse writhing assay. In
 rat infusion tests, the phenethyl analog I; (R₁ = H, R₂ =
 CH₂CH₂Ph, HBr) [47025-61-0] had a well-balanced
 analgesic-antagonist profile devoid of phys. dependence liability.
 Structure-activity relations are discussed.
 IT 61320-99-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and Wolff-Kishner reduction of)
 RN 61320-99-8 CA
 CN 2-Azabicyclo[3.2.1]octan-8-one, 5-(3-methoxyphenyl)-2-methyl- (9CI) (CA
 INDEX NAME)

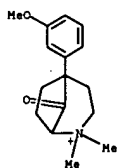


L5 ANSWER 44 OF 55 CA COPYRIGHT 2005 ACS on STN
 87:167854 CA
 TITLE: Azabicycloalkanes as analgetics. VI.
 5-Phenyl-2-azabicyclo[3.2.1]octanes
 AUTHOR(S): Noguchi, Katsuyuki; Takeda, Mikio; Nurimoto, Seichi
 CORPORATE SOURCE: Res. Lab., Tanabe Seiyaku Co., Ltd., Saitama, Japan
 SOURCE: Chemical & Pharmaceutical Bulletin (1977), 25(5),
 890-6
 CODEN: CPBTAL; ISSN: 0009-2363
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 87:167854
 GI



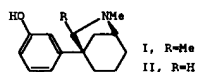
AB The title compound I, a benzomorphan analog, was prepared to study
 structure-activity relationships of the partial agonist activity of
 phenylazabicycloalkane analgesics. Cyclizing the aminoketone II (R =
 3-MeOC₆H₄) gave the 8-oxo derivative of I which was reduced under
 Wolff-Kishner conditions. Alternatively, intramol. Michael reaction of
 the aminocyclopentanone generated in situ by hydrolysis of urethane III
 gave the 6-oxo derivative IV (R = 3-MeOC₆H₄), also convertible to I. The
 keto
 enamines V (R₁ = H, OMe), obtained by Hg(OAc)₂ oxidation of the dehydro
 derivs., were cyclized to IV (R = Ph, 3-MeOC₆H₄) by heating them with
 aqueous
 HOAc. I was analgesically inactive but exhibited narcotic antagonistic
 activity comparable to pentazocine.
 IT 61320-97-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and cyclization of)
 RN 61320-97-6 CA
 CN 2-Azabicyclo[3.2.1]octane, 5-(3-methoxyphenyl)-2,2-dimethyl-8-oxo-,
 bromide (9CI) (CA INDEX NAME)

L5 ANSWER 44 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)

● Br⁻

L5 ANSWER 45 OF 55 CA COPYRIGHT 2005 ACS on STN

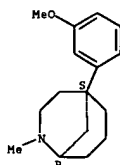
ACCESSION NUMBER: 86:50482 CA
 TITLE: Azabicycloalkanes as analgesics. 3. Structure-activity relations of 1-phenyl-6-azabicyclo[3.2.1]octanes and absolute stereochemistry of (+)-1-(3-hydroxyphenyl)-6-methyl-6-azabicyclo[3.2.1]octane and its 7-endo-methyl derivative
 AUTHOR(S): Takeda, Mikio; Inoue, Hirozumi; Noguchi, Katsuyuki; Honma, Yasushi; Kawamori, Masatoshi; Tsukamoto, Goro; Yamawaki, Yasuhiko; Saito, Seichi; Aoe, Keiichi; et al.
 CORPORATE SOURCE: Res. Lab., Tanabe Seiyaku Co. Ltd., Japan
 SOURCE: Journal of Medicinal Chemistry (1977), 20(2), 221-8
 CODEN: JMCMAH; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 86:50482
 GI



AB A series of 53 1-phenyl-6-azabicyclo[3.2.1]octanes was tested for analgesic and narcotic antagonist activities and structure-activity relations were studied. (+)-1-(3-Hydroxyphenyl)-6,7-dimethyl-6-azabicyclo[3.2.1]octane-HBr [(+)-I-HBr] [61098-47-3] had the profile of a well-balanced antagonist-analgesic agent with very mild phys. dependence capacity. The absolute stereochem. of the enantiomer with analgesic activity, (+)-I-HCl [60933-48-4], was determined by x-ray study and chemical transformation to known compds., and was stereochem. correlated to the active 7-demethyl derivative [(+)-II-HCl] [61176-36-1]. The relation of analgesic and narcotic activity to configuration, and structural and stereochem. correlations between I and II and known antagonist-analgesics are discussed.
 IT 51596-44-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and O-demethylation of)
 RN 51596-44-2 CA
 CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)-2-methyl-, hydrobromide, (1R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 45 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)



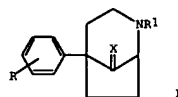
● HBr

L5 ANSWER 46 OF 55 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 86:29671 CA
 TITLE: Azabicycloalkanes
 INVENTOR(S): Ong, Helen Hu; Anderson, Vernon Brian
 PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
 SOURCE: Ger. Offen., 45 pp.
 CODEN: GWCKBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

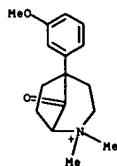
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2610702	A1	19761007	DE 1976-2610702	19760313
IL 49034	A1	19800229	IL 1976-49034	19760213
ES 446051	A1	19770916	ES 1976-446051	19760313
NL 7602681	A	19760922	NL 1976-2681	19760315
SE 7603355	A	19760921	SE 1976-3355	19760317
FI 7600727	A	19760921	FI 1976-727	19760318
FR 2304331	A1	19761015	FR 1976-7839	19760318
FR 2304331	B1	19800718		
AU 7612157	A1	19770922	AU 1976-12157	19760318
GB 1538152	A	19790117	GB 1976-10931	19760318
DK 7601206	A	19760921	DK 1976-1206	19760319
NO 7600976	A	19760921	NO 1976-976	19760319
JP 51122046	A2	19761025	JP 1976-30720	19760319
ZA 7601715	A	19770427	ZA 1976-1715	19760319
AT 7602070	A	19800515	AT 1976-2070	19760319
AT 360010	B	19801210		
CA 1080705	A1	19800701	CA 1976-248298	19760319
BE 839886	A1	19760922	BE 1976-165443	19760322
FR 2346002	A1	19771028	FR 1976-33965	19761110
FR 2346002	B1	19800328		

PRIORITY APPLN. INFO.:
 GI US 1975-560510 A 19750320



AB Azabicycloalkanes (I; R = 3-OH, 4-OH, 3-MeO, 4-MeO, 3-AcO; R1 = e.g., H, Me, Et, CN, PhCH2CH2; X = O, H2), useful as analgesics (no data), are prepared by cyclization of 5-bromo-2-[2-(dialkylamino)ethyl]-2-phenylcyclopentanones, followed by various standard procedures. Thus, treatment of 5-bromo-2-[2-(dimethylamino)ethyl]-2-(3-methoxyphenyl)cyclopentanone with Et2O and NH4OH, followed by refluxing 2 hr in Me2CO, gives the methobromide of I (R = 3-MeO, R1 = Me, X = O).
 IT 61320-97-6P
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)
 RN 61320-97-6 CA

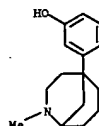
L5 ANSWER 46 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)
 CN 2-Azonabicyclo[3.2.1]octane, 5-(3-methoxyphenyl)-2,2-dimethyl-8-oxo-,
 bromide (9CI) (CA INDEX NAME)



● Br⁻

L5 ANSWER 47 OF 55 CA COPYRIGHT 2005 ACS on STN

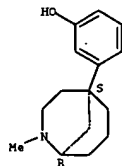
82:51660 CA
 TITLE: Improved synthesis and additional pharmacology of the
 potent analgesic (-)-5-m-hydroxyphenyl-2-methylmorphan
 Rogers, Michael E.; May, Everette L.
 AUTHOR(S): Natl. Inst. Arthritis, Metab. Dig. Dis., Natl. Inst.
 CORPORATE SOURCE: Health, Bethesda, MD, USA
 SOURCE: Journal of Medicinal Chemistry (1974), 17(12), 1328-30
 CODEN: JMCMAH; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA Issue.
 AB The title compound (I) [27107-68-2] (16 mg/kg/day s.c.) produced
 very slight phys. dependence in Rhesus monkeys. Nalorphine and naloxone
 did not precipitate withdrawal symptoms in monkeys receiving I. At 32
 mg/kg, I
 produced convulsions in monkeys. The 24-hr LD50 of I in mice was 137
 mg/kg s.c. The yield of I in the previously reported synthesis (E. L. May
 and J. G. Murphy, 1955) was improved by changing the conditions for
 dimethylaminoethylation of 2-m-methoxyphenylcyclohexanone (II)
 [15547-89-4] and improving the resolution procedure. An alternative
 synthesis of I was described in which II was alkylated with Et
 bromoacetate [105-36-2], converted to the keto aldehyde, cyclized, and
 converted by several steps including a Beckmann rearrangement via
 3-oxo-5-m-methoxyphenyl-2-azabicyclo[3.3.1]nonane to I.
 IT 27107-68-2P
 RL: SYN (Synthetic preparation); PREP (Preparation)
 (preparation and analgesic activity of, dependence in relation to)
 RN 27107-68-2 CA
 CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)



L5 ANSWER 48 OF 55 CA COPYRIGHT 2005 ACS on STN

82:25673 CA
 TITLE: Stereochemistry and absolute configuration of the
 analgesic agonist-antagonist (-)-5-m-hydroxyphenyl-2-
 methylmorphan
 Cochran, Todd G.
 AUTHOR(S): Sch. Pharm., Duquesne Univ., Pittsburgh, PA, USA
 CORPORATE SOURCE: Journal of Medicinal Chemistry (1974), 17(9), 987-9
 SOURCE: CODEN: JMCMAH; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA Issue.
 AB Addnl. data considered in abstracting and indexing are available from a
 source cited in the original document. The absolute configuration of
 (-)-5-m-hydroxyphenyl-2-methylmorphan-HBr (I-HBr) [53467-24-6]
 was established as 1R, 5S by single-crystal x-ray anal. Both rings of the
 azabicyclononane system exist in chair conformations with the Ph and Me
 substituents equatorial. The distance between the cationic N and the
 aromatic ring is 5.66 Å. The relation between conformation and activity
 and receptor interaction was discussed.
 IT 53467-24-6
 RL: PRP (Properties)
 (absolute configuration of)
 RN 53467-24-6 CA
 CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrobromide, (1R)-
 (9CI) (CA INDEX NAME)

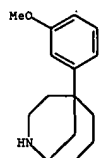
Absolute stereochemistry. Rotation (-).



● HBr

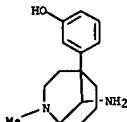
L5 ANSWER 49 OF 55 CA COPYRIGHT 2005 ACS on STN

80:91126 CA
 TITLE: Phenylmorphans agonists-antagonists
 Ong, Helen H.; Ohishi, Tokuro; May, Everette L.
 AUTHOR(S): Natl. Inst. Arthritis, Metab. Dig. Dis., Natl. Inst.
 CORPORATE SOURCE: Health, Bethesda, MD, USA
 SOURCE: Journal of Medicinal Chemistry (1974), 17(1), 133-4
 CODEN: JMCMAH; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB (+)-5-(4-hydroxyphenyl)-2-propylmorphans-HBr (I) [51264-07-4],
 (+)-2-allyl-5-(4-hydroxyphenyl)morphans-HBr (II) [51264-08-5],
 and (+)-2-(cyclopropylmethyl)-5-(4-hydroxyphenyl)morphans-HBr (III) [51264-09-6] and the corresponding racemates were prepared and tested
 as analgesics. I and II were prepared by alkylation of (+)-5-(4-
 hydroxyphenyl)morphans (IV) [51264-10-9], while III was prepared by
 acylation of IV, followed by LiAlH₄ reduction. The analgesic activities of
 I,
 II, and III were 2-3 times higher than the corresponding racemates in the
 Nilsen test. With the hot plate test, I was 3 times more potent than its
 racemate. Analgesic and antagonist activities of the phenylmorphans
 derivative
 isomers were related to nalorphine-HCl [57-29-4], pentazocine-HCl
 [2276-52-0], and morphine sulfate [64-31-3].
 IT 51596-46-4
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (demethylation of)
 RN 51596-46-4 CA
 CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)-, hydrobromide (9CI) (CA
 INDEX NAME)



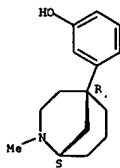
● HBr

L5 ANSWER 50 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 76:140587 CA
 TITLE: Photocyclizations. II. Synthesis of iminoethanophenanthridine (seven-membered ring) homologs
 AUTHOR(S): Ong, Helen M.; May, Everette L.
 CORPORATE SOURCE: Natl. Inst. Arthritis Metab. Dis., Natl. Inst. Health, Bethesda, MD, USA
 SOURCE: Journal of Organic Chemistry (1972), 37(5), 712-16
 CODEN: JOCEAH; ISSN: 0022-3263
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA issue.
 AB Photolysis of 9-cis-chloroacetamino-5-(m-hydroxyphenyl)-2-methyl-2-azabicyclo[3.3.1]nonane gave both ortho and para ring closure to propanopyridobenzazepinones (I and II) whose structures were deduced from mass and NMR spectral data and by chemical evidence.
 IT 32969-96-3P
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)
 RN 32969-96-3 CA
 CN Phenol, 3-(9-amino-2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)



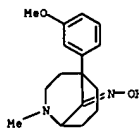
L5 ANSWER 52 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 73:87772 CA
 TITLE: Optical isomers of miscellaneous strong analgetics
 AUTHOR(S): May, Everette L.; Takeda, Mikio
 CORPORATE SOURCE: Nat. Inst. of Arthritis and Metab. Dis., Nat. Inst. of Health, Bethesda, MD, USA
 SOURCE: Journal of Medicinal Chemistry (1970), 13(5), 805-7
 CODEN: JMCHAM; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA issue.
 AB Optical isomers of α-5,9-diethyl-2'-methoxy- (Ia), α-2,5-dimethyl-9-ethyl-2'-hydroxy- (Id), and 2'-hydroxy-2-methyl-6,7-benzomorphans (Ic) and of 5-(m-hydroxyphenyl)-2-methylmorphans (II) have been prepared and compared with parent racemates in analgetic activity, physical dependence capacity, and antagonistic behavior. Racemate Ic, (+)-Ic, (-)-Ic and (-)-II, have morphine-like analgetic and nalorphine-like antagonistic action. Ia was prepared from Ib.
 IT 27107-49-9P
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)
 RN 27107-49-9 CA
 CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



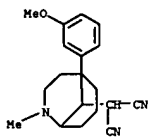
● HCl

L5 ANSWER 51 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 76:85730 CA
 TITLE: Iminoethanophenanthridines by the Pictet-Spengler reaction
 AUTHOR(S): Ong, Helen M.; May, Everette L.
 CORPORATE SOURCE: Natl. Inst. Arthritis Metab. Dis., Natl. Inst. Health, Bethesda, MD, USA
 SOURCE: Journal of Heterocyclic Chemistry (1971), 8(6), 1007-9
 CODEN: JHICAD; ISSN: 0022-152X
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA issue.
 AB Pictet-Spengler cyclization of 9-cis-amino-5-(m-methoxyphenyl)-2-methyl-2-azabicyclo[3.3.1]nonane (I) gave 2,3,4,4a,5,6-hexahydro-9-methoxy-3-methyl-1H-4,10b-propanobenzo[c][1,7]naphthyridine (II), derivs. of which were weakly analgesic. Thus, I was refluxed 4 hr in EtOH-HCHO-HCl to give 82% II. ZHCl, which was converted to the O-demethyl derivative (III) with HBr. III was treated with cyclopropylcarbonyl chloride-Et3N and the product reduced with LiAlH4 to give the 5-(cyclopropylmethyl) derivative (IV) of
 III. The hot-plate test showed that III and IV possessed approx. 14% the analgesic activity of codeine.
 IT 35190-78-4P
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)
 RN 35190-78-4 CA
 CN 2-Azabicyclo[3.3.1]nonan-9-one, 5-(3-methoxyphenyl)-2-methyl-, oxime (9CI) (CA INDEX NAME)



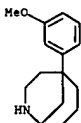
L5 ANSWER 53 OF 55 CA COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 53:122365 CA
 ORIGINAL REFERENCE NO.: 53:22043e-1
 TITLE: Structures related to morphine. X. A position isomer of (+)-3-hydroxy-N-methylmorphinan (Racemorphan)
 AUTHOR(S): May, Everette L.
 CORPORATE SOURCE: Natl. Inst. of Arthritis and Metabolic Diseases, Bethesda, MD
 SOURCE: Journal of Organic Chemistry (1959), 23, 947-9
 CODEN: JOCEAH; ISSN: 0022-3263
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB cf. C.A. 52, 5154c. Converting 4.0 g. HCl salt of 5-(m-methoxyphenyl)-2-methyl-9-oxomorphans (I) to I in dilute aqueous NH3-Et2O, refluxing 1 hr. with 1.2 g. CH2(CN)2, 0.3 g. NH4OAc, 0.6 ml. HOAc, and 8 ml. C6H6 with azeotropic H2O removal, adding Et2O and HCl, and crystallizing the precipitate from warm acetone gave 84% 9-dicyanomethylene-2-methyl-5-(m-methoxyphenyl)morphans (II).HCl, m. 208-12° (decomposition). Hydrogenation (1 atmospheric) of 3.9 g. II.HCl in MeOH over PtO2 2 hrs., concentration to 8 ml., and cooling gave 46% 9-dicyanomethyl analog (III), m. 246-8° (decomposition). Refluxing 1.8 g. III in 4 ml. H2O and 17 ml. concentrated HCl 16 hrs., concentrating in vacuo, extracting the residue with 1:1 EtOH-Me2CO from 84% NH4Cl, concentrating, washing in Et2O with 10% NaOH, and distilling gave 0.9 g. viscous oil, converted in Me2CO-dry HCl to 35% 1,2,3,9,10,10a-hexahydro-6-methoxy-11-methyl-9-oxo-1,4a-4H-iminoethanophenanthrene (IV).HCl, m. 261-3°, λ 5.96 μ (Nujol). The filtrate gave 0.11 g. C17H22ClNO2.0.5H2O, probably the 6-HO analog of IV, m. 191-8°, λ 2.17, 2.60, 3.36 μ, n 22,000, 13,000, 5800, soluble in NaOH. 1,2,3,9,10,10a-Hexahydro-6-methoxy-11-methyl-1,4a-4H-iminoethanophenanthrene (V) (98% from 0.6 g. IV, 0.5 g. KOH, 0.5 ml. 95% NH4, and 5 ml. triethylene glycol 16 hrs. at 170-180° and 10 min. at 200°) m. 93-4°; methiodide m. 265-7° (froth); HCl salt, C18H26ClNO.0.5-H2O, no m.p. given. Refluxing 0.4 g. V and 3 ml. HBr 0.5 hr., digesting the residue with 5 ml. EtOH, and cooling gave 83% 6-HO analog; HBr salt m. 268-72°; free base m. 246-8° (froth). Crystallization of the HBr salt from EtOH gave prisms, m. 150-5°, containing 1 mole solvate EtOH. Refluxing 0.15 g. (+)-3-methoxy-N-methylmorphinan-MeI in 5 ml. 10% NaOH 2 hrs., hydrogenating in MeOH over PtO2 10 min., and treating the residue with saturated picric acid gave 79% 4a-(2-dimethylaminoethyl)-6-methoxy-1,2,3,4,4a,9,10,10a-octahydrophenanthrene picrate, m. 158-9° also prepared in 31% yield by heating 0.09 g. V.MeI, 0.4 g. KOH, 4 ml. H2O, and 1 ml. triethylene glycol 3 hrs. at 135-40° and distilling the Et2O-soluble product at 150°/0.5 mm.
 IT 110392-61-5, 2-Azabicyclo[3.3.1]nonane-9-malononitrile, 5-(m-methoxyphenyl)-2-methyl-, hydrochloride (preparation of)
 RN 110392-61-5 CA
 CN 2-Azabicyclo[3.3.1]nonane-9-malononitrile, 5-(m-methoxyphenyl)-2-methyl-, hydrochloride (6CI) (CA INDEX NAME)

L5 ANSWER 53 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)



● HCl

L5 ANSWER 54 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)
 (derivs.)
 RW 111162-06-2 CA
 CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 54 OF 55 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 52:11165 CA
 ORIGINAL REFERENCE NO.: 52:2032d-1
 TITLE: Structures related to morphine. VI. N-Phenylethyl derivatives of some phenyl- and benzomorphans
 AUTHOR(S): May, Everett L.
 CORPORATE SOURCE: Natl. Insts. of Health, Bethesda, MD
 SOURCE: Journal of Organic Chemistry (1956), 21, 899-901
 CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB cf. C.A. 50, 15560h. N-Me derivs. were converted to N-phenylethyl analogs. These were shown two to three times less effective than the respective N-Me counterparts in producing analgesia in mice, contrary to results obtained with meperidine and race-morphin types. To 1.2 g. BrCN in 7 ml. dry CHCl₃ was added 2.4 g. 5-(m-methoxyphenyl)-2-methylmorphane (I) in 10 ml. CHCl₃ during 45 min. while stirring, refluxed 3 hrs., evaporated to dryness in vacuo, the residue dissolved in EtOH, refluxed briefly, evaporated to dryness, 10 ml. EtOAc added to recover 0.5 g. I-HBr, m. 158-62°. Filtrate freed from EtOAc in vacuo, the residue and 45 ml. 6% HCl refluxed overnight, cooled to 0°, basified with 10% KOH, the liberated oil dried in ether, 32% HBr-AcOH added, kept overnight at 0°, the semisolid washed with ether, and triturated with EtOAc containing a little acetone gave 1.3 g. 2-(m-methoxyphenyl)morphane-HBr (II), m. 127-30°, 67% yield (with 0.3 g. from filtrate), m. 162-5° (acetone-ether); picrate, yellow prisms, m. 162-5° (EtOH). Phenylacetyl chloride (1.0 ml.) added during 3-5 min. to a stirred mixture of 1.0 g. II, 1.5 g. K₂CO₃, 5 ml. H₂O, and 15 ml. MeOH, stirred 1 hr., diluted with 3 volume H₂O, extracted with ether, the extract washed with dilute HCl and dilute NaOH, dried, and evaporated to dryness gave 1.5 g. sirup, which in 20 ml. dry ether treated gradually with 20 ml. 1.4M ethereal LiAlH₄, refluxed overnight, treated carefully with 10-15 ml. H₂O, the ether decanted from residual hydrides which were washed three times, combined ether portions dried, and acidified with 32% HBr-AcOH gave 1.1 g. 5-(m-methoxyphenyl)-2-(2-phenylethyl)morphane-HBr (III), leaflets, m. 209-11° (acetone). III (1.1 g.) refluxed in 7 ml. 48% HBr 30 min., evaporated to dryness, and the residue triturated with absolute EtOH containing a little acetone gave 0.8 g. 5-(m-hydroxyphenyl)-2-(2-phenylethyl)morphane-HBr, m. 274-7.5° (from MeOH). To 0.5 g. BrCN in 3 ml. CHCl₃ was added 0.9 g. 5-phenyl-2-methyl-morphane in 5 ml. CHCl₃ during 1 hr., refluxed 3 hrs., evaporated to dryness, dissolved in a little EtOH, refluxed briefly, evaporated to dryness, and the residual sirup with 20 ml. 6% HCl refluxed overnight gave an almost clear solution which was shaken with ether, the aqueous layer basified with 10% NaOH, the oil in ether dried and brought to reaction with phenylacetyl chloride as described above. The resultant amide (1.3 g.) reduced with 15 ml. 1.4M ethereal LiAlH₄ gave 0.8 g. 5-phenyl-2-(2-phenylethyl)morphane-HBr, glittering plates, m. 264-7° (EtOH); picrate, yellow cubes, m. 184-6° (acetone-EtOH). By the same way, 1.6 g. 2,5-dimethyl-5,7-benzomorphane yielded 1.1 g. 5-methyl-2-(2-phenylethyl)-6,7-benzomorphane-HCl, m. 249-7° (decomposition) (absolute EtOH); picrate, m. 142-6° (EtOH).
 IT 111162-06-2, 2-Azabicyclo[3.3.1]nonane, 5-(m-methoxyphenyl)-

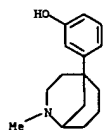
L5 ANSWER 55 OF 55 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 50:44580 CA
 ORIGINAL REFERENCE NO.: 50:8635d-1,8636a
 TITLE: Structures related to morphine. IV. m-Substituted phenylcyclohexane derivatives
 AUTHOR(S): May, Everett L.; Murphy, James G.
 CORPORATE SOURCE: Natl. Inst. of Health, Bethesda, MD
 SOURCE: Journal of Organic Chemistry (1955), 20, 1197-1201
 CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 OTHER SOURCE(S): CASREACT 50:44580
 AB cf. C.A. 50, 4165a. 1-(2-Dimethylaminoethyl)-1-(m-hydroxyphenyl)cyclohexane (I) and 5-(m-hydroxyphenyl)-2-methylmorphane (II) have been prepared to be tested for their analgesic activity. Stirring 14 g. 2-(m-methoxyphenyl)-1-nitro-4-cyclohexene in 105 cc. 95% EtOH 1 h. in a N atmosphere with 90 cc. alc. NaOEt (from 3 g. Na), then adding (40 min.) 240 cc. H₂O, 180 cc. 95% EtOH, and 72 cc. concentrated HCl at -5° to 0° with stirring, stirring the mixture another hr. at 0° and 0.5 h. at 20°, pouring it into 1.2 l. ice-salt-H₂O, extracting it quickly with Et₂O, and evaporating the washed (saturated NaHCO₃, H₂O) Et₂O extract in vacuo under N give 12.2 g. residue which is hydrogenated 40 min. in 25 cc. MeOH with 3 g. 5% Pd-BaSO₄, giving 83% 2-(m-methoxyphenyl)cyclohexanone (III), b.p. 0.2 135-45° (air bath temperature), n_D20 1.5497. Adding (5-10 min.) 8.8 g. III in 60 cc. C₆H₆ to 1.7 g. NaNH₂ in 40 cc. refluxing C₆H₆, refluxing the solution 0.5-1 h., adding (30-45 min.) 4.8 g. CH₂ClCH₂Me₂ in 60 cc. C₆H₆, refluxing the mixture 20 h. with stirring, washing it with H₂O, extracting it with dilute HCl, warming the acid extract slightly, washing it with Et₂O, making it basic with NH₄OH, extracting with Et₂O, and treating the dried Et₂O extract with dry HCl give 24% 2-(2-dimethylaminoethyl)-2-(m-methoxyphenyl)cyclohexanone-HCl (IV), prisms, m. 165.5-6.5°, and, from the mother liquors, 5.2 g. unchanged III. Heating 0.5 g. IV, 0.5 cc. 95% N₂H₄, 0.5 g. KOH, and 5 cc. triethylene glycol 6 h. at 180-210° and treating the reduction product with 32% HBr-AcOH give 90% 2-(2-dimethylaminoethyl)-1-(m-methoxyphenyl)cyclohexane-HBr (V), prisms, m. 167-8.5°. Refluxing 0.6 g. V 0.5 h. with 2.5 cc. 48% HBr and evaporating the solution in vacuo give 87% I-HBr, needles, m. 178-9° (HCl salt, needles, m. 191.5-3°). Treating 0.5 g. I-HBr in 0.5 cc. Ac₂O and 1 cc. C₆H₅SO₃ 1 h. at 25°, diluting the mixture with Et₂O, and keeping it overnight at 5° give 0.55 g. 1-(m-acetoxymethyl)-1-(2-dimethylaminoethyl)cyclohexane-HBr, needles, m. 138-8.5°. Converting 12 g. IV into 12.4 g. HBr salt and treating the latter in 140 cc. refluxing AcOH with 6 g. Br in 50 cc. AcOH, diluting the mixture with 500 cc. Et₂O, and keeping it overnight at -6° give 14.5 g. 6-Br derivative-HBr of IV, needles, m. 184-5°, which, treated 1-2 h. in 35 cc. H₂O with 4 cc. concentrated NH₄OH, gives 90% 5-(m-methoxyphenyl)-2-methyl-9-oxomorphane (VI) methobromide (VII), thick plates, m. 249-50° (decomposition). Dry distillation of 10.2 g. VII at 210-25°/0.5 mm. gives 89% VI-HCl, plates, m. 203-5° (decomposition). Heating 7.7 g. VI-HCl in 50 cc. triethylene glycol with 7 cc. 95% N₂H₄ and 7 g. KOH 5.5 h. at 175° and 0.5 h. at 190° gives 90% 5-(m-methoxyphenyl)-2-methylmorphane-HBr, oblong plates, m. 165-7°, which (7.7 g.), refluxed with 30 cc. 48% HBr, gives 60% II-HBr, m. 171-2° (free base, m. 156-7.5°; m-Ac derivative-HBr, 100%, small prisms, m.

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LS ANSWER 55 OF 55 CA COPYRIGHT 2005 ACS on STN (Continued)
162.5-3.5'). The results of the pharmacol tests of these compds.
are given in a table.
IT 27107-68-2, 2-Azabicyclo[3.3.1]nonane, 5-(m-hydroxyphenyl)-2-
methyl-
(and derivs.)
RN: 27107-68-2 CA
CN: Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)



10/798,664

=> d his

(FILE 'HOME' ENTERED AT 14:42:19 ON 13 JUL 2005)

FILE 'REGISTRY' ENTERED AT 14:42:24 ON 13 JUL 2005

L1 STRUCTURE UPLOADED

L2 17 S L1 SAM

FILE 'CA' ENTERED AT 14:42:40 ON 13 JUL 2005

L3 17 S L2

FILE 'REGISTRY' ENTERED AT 14:42:49 ON 13 JUL 2005

L4 431 S L1 FULL

FILE 'CA' ENTERED AT 14:42:55 ON 13 JUL 2005

L5 55 S L4

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---Logging off of STN---

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Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 14:43:37 ON 13 JUL 2005